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Cullis et al.

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[54] **METHOD AND SYSTEM FOR FRACTIONATING A QUANTITY OF BLOOD INTO THE COMPONENTS THEREOF**

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[51] **Int. Cl.**[2] **B04B 15/12**

[52] **U.S. Cl.** ..... **233/14 R**; 233/26; 128/214 D

[58] **Field of Search** ..... 233/14 R, 14 A, 19 R, 233/19 A, 27, 26, 21, 22; 128/214 R, 2 F, 214 D

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,655,123	4/1972	Judson et al.	233/21
3,967,777	7/1976	Canevari	233/19 R
3,982,691	9/1976	Schlutz	233/21 X
4,091,989	5/1978	Schlutz	233/27 X

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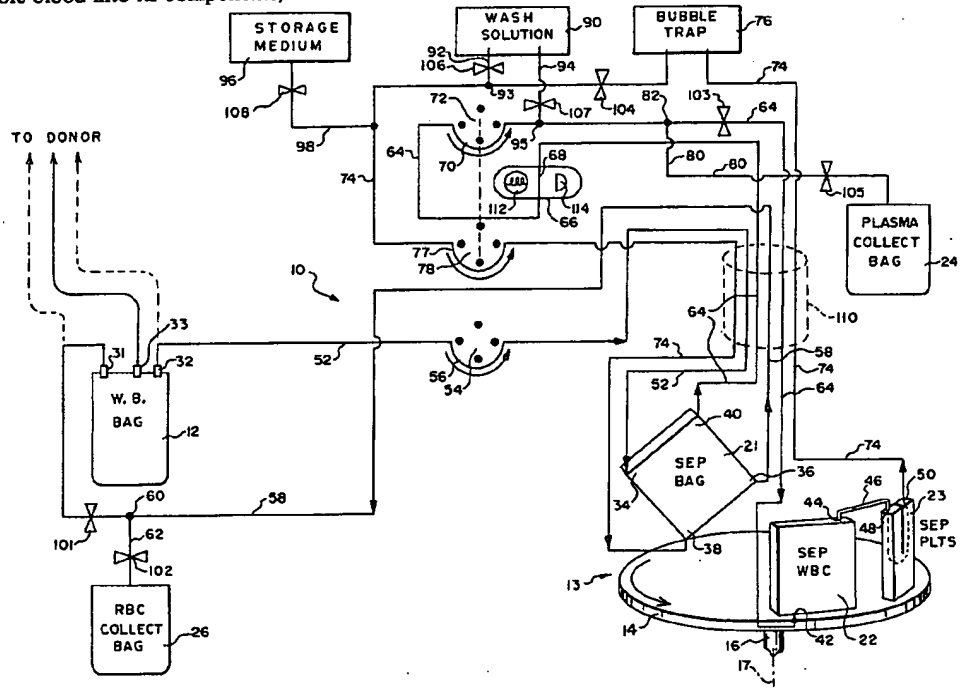
[57] **ABSTRACT**

The method, and system for carrying out the steps of the method, are utilized in taking whole blood from a supply of blood withdrawn from a donor or from a previously banked supply of whole blood in a container, centrifuging the blood in a centrifuge device to separate the whole blood into its components, and then collecting the components, namely red blood cells, white blood cells, platelets and plasma. The fractionation of the whole blood in the centrifuge device takes place in first, second and third separation chambers. The first chamber has a square shape and is positioned in the centrifuge device in a diamond position. Each corner of the first separation chamber has an opening. Whole blood is pumped into one side corner opening and red blood cells are withdrawn from the other side corner opening and returned to the container for recirculation through the first chamber. White blood cells, platelets and plasma are withdrawn from the upper corner opening and passed through the second chamber wherein white blood cells are separated by centrifugal force. The plasma and platelets are then withdrawn from the second chamber and passed through the third chamber wherein the platelets are separated from the plasma by centrifugal force. The plasma exiting from the third separation chamber is passed back into the bottom corner of the first chamber to cause a flow of plasma across the flow of whole blood and red blood cells to elute white blood cells and plateletstherefrom and to wash the red blood cells. By appropriate operation of electromechanically controlled clamps associated with tubing carrying the various blood components, plasma can be siphoned off into a plasma collection receptacle located outside the centrifuge device. After the red blood cells have been recirculated several times through the first separation chamber, the red blood cells then can be directed to a red blood cell collection receptacle by operation of other electromechanically controlled clamps.

86 Claims, 6 Drawing Figures



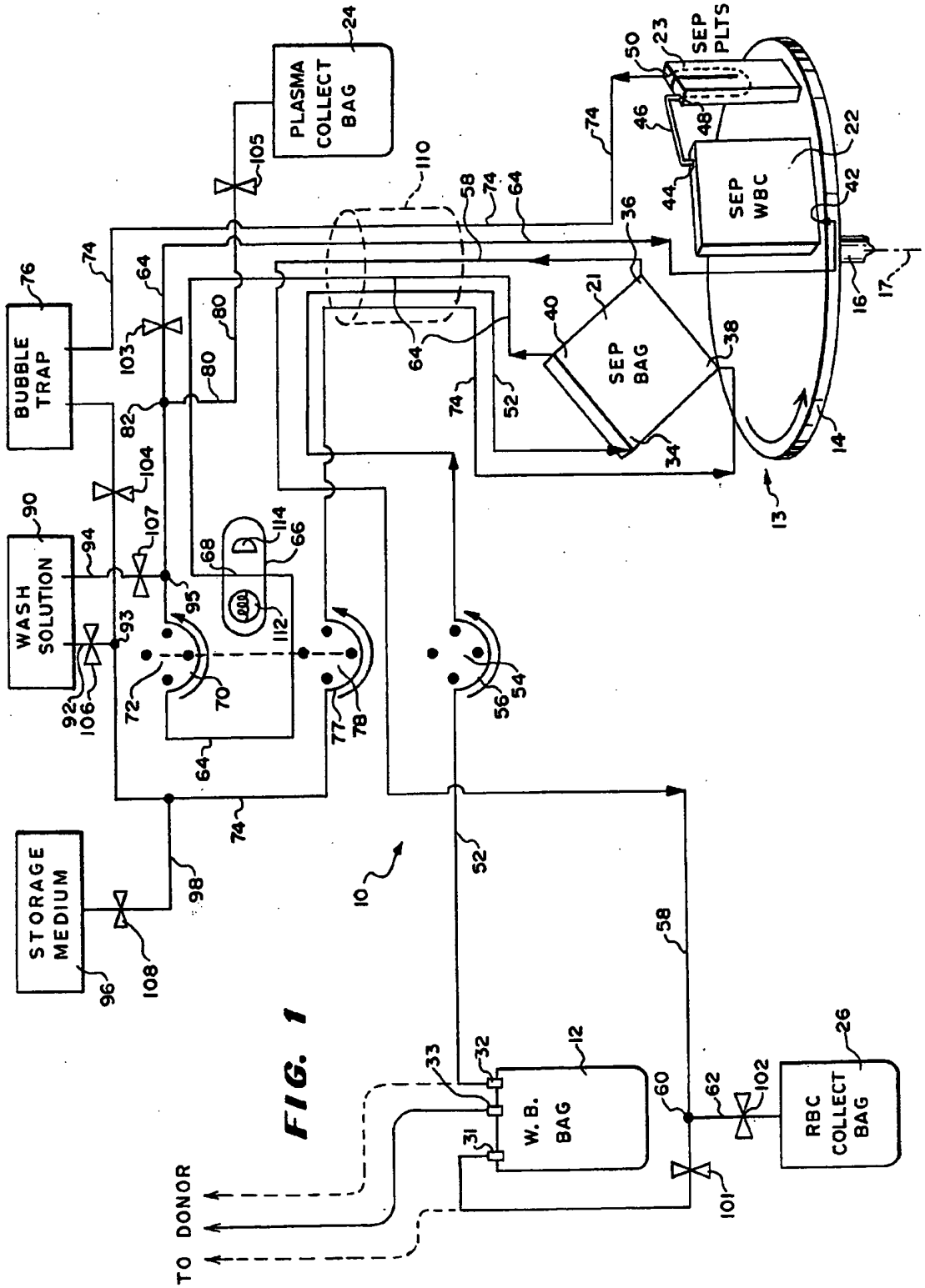

PLASMA COLLECT BAG
SEP PLTS
SEP WBC
SEP BAG
BUBBLE TRAP
WASH SOLUTION
STORAGE MEDIUM
W. B. BAG
RBC COLLECT BAG
TO DONOR

FIG. 1

FIG. 2

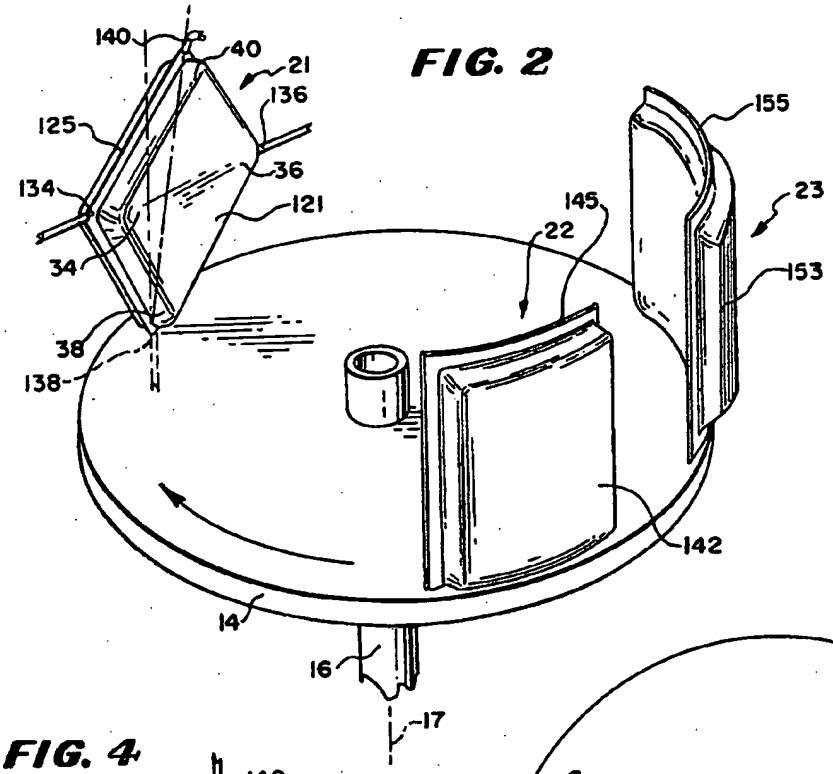


FIG. 3

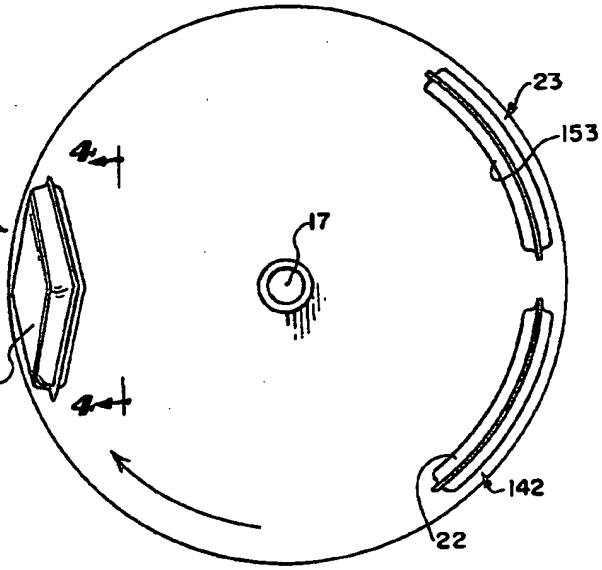


FIG. 4

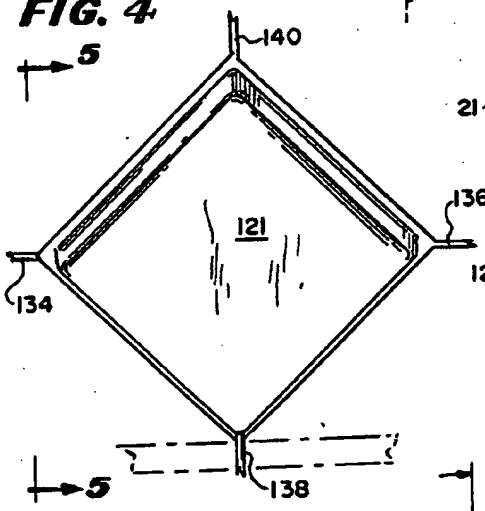
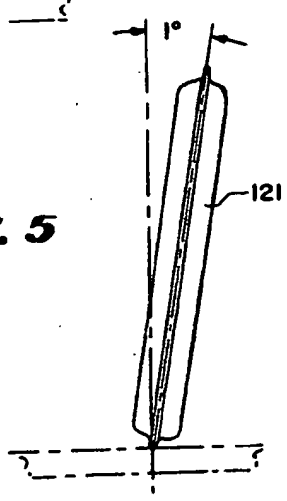


FIG. 5



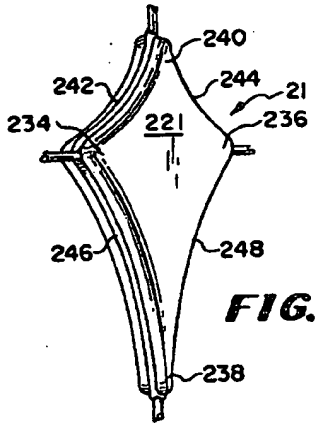


FIG. 6

METHOD AND SYSTEM FOR FRACTIONATING A QUANTITY OF BLOOD INTO THE COMPONENTS THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

This application is related to and incorporates herein by reference, copending application Ser. No. 843,222 filed Oct. 18, 1977 and entitled: METHOD AND APPARATUS FOR PROCESSING BLOOD and copending application Ser. No. 843,296 filed Oct. 18, 1977 entitled: CENTRIFUGAL LIQUID PROCESSING SYSTEM.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method and system for fractionating whole blood into its components and to a separation chamber within which blood is fractionated.

2. Description of the Prior Art

Heretofore, various methods and systems have been proposed for fractionating whole blood into the components thereof. Such prior art methods and systems have involved intervivos blood processing in which whole blood is taken from a live donor, separated within a processing system into its constituent components and a desired component (or components) is segregated for collection followed by returning the remaining blood fluid to the donor.

Whenever a live donor is supplying the blood to be fractionated there are always hazards involved and various protective steps have to be taken to insure that no harm comes to the donor. Examples of the various safeguards that need to be taken are explained in greater detail in the related co-pending application Ser. No. 843,222 referred to above. Also, in order to collect large numbers of white blood cells and platelets a healthy donor is usually required. This process for processing whole blood taken from a live donor is referred to as cytopheresis or plasmapheresis.

One previously proposed closed system for fractionating whole blood utilizes four plastic bags interconnected by plastic tubing. All the bags are placed in a centrifuge device and whole blood in a first bag is then centrifuged. Red blood cells collect at the bottom of the bag, white blood cells in the middle, and plasma collects at the top. A "plasma express" tubing which is closed inside is connected to the top of the bag and has an "in-line" cannula therein. After the first centrifuging, the cannula is moved in the tubing to open same and plasma and platelets are expressed from the first bag into a second bag by applying pressure to the first bag. Then the second bag is centrifuged to separate plasma from platelets and followed by expressing the platelets and plasma into respective third and fourth bags. This system requires operator intervention and takes several hours to complete. Also the efficiency of the separation is approximately 50%.

As will be described in greater detail hereinafter, the method and system of the present invention enables one automatically and efficiently to fractionate in a closed, sterile environment, previously collected stored quantities of whole blood or blood collected directly from a donor into the components thereof. It is estimated that by utilizing the blood fractionating method and system of the present invention, three pints of banked whole blood can be processed automatically in a closed sterile environment to produce quantities of the fractionated components thereof equivalent to the quantities of these components that would be obtained by extended cytopheresis or plasmapheresis and with an efficiency of fractionation of 90% or better.

Another advantage of the blood fractionating method and system of the present invention is that a donor can supply quantities or whole blood at different times, i.e., in batches—pints of whole blood stored in blood bags, and then each whole blood bag can be processed by the method and system of the present invention at any desired time without requiring a donor to be connected to the apparatus.

Also, and as will be explained in greater detail hereinafter, a further advantage of the method and system of the present invention is that any given quantity of whole blood can be more completely and better utilized by dividing it into desired components and distributing the components to different recipients. The economy arises because any given transfusion is made for the purpose of replenishing a single component, for example only red blood cells are needed, and the other components such as white blood cells, platelets and plasma will not generally contribute to the treatment and many times are injurious by virtue of their volume, particularly in the case of plasma, or by virtue of their incompatible antigenic nature, particularly in the case of white blood cells. Also, infusion of any blood component not actually required by the recipient is a waste of a vital and hard to obtain resource.

Moreover, as will be explained in greater detail hereinafter, the present system provides for the removal of certain plasma proteins, in particular, Immunoglobulin A, by removing the plasma and washing the red blood cells. In other words, removal of the plasma from the red cells removes Immunoglobulin A which has been shown to sensitize recipients and can be a cause of transfusion reactions. Sensitizing is a biological description of the process whereby an individual recognizes an antigen and gets an immune response, such as with allergies or hay fever.

SUMMARY OF THE INVENTION

According to the invention there is provided a method for fractionating a given amount of whole blood into several of its components, including the steps of: separating the whole blood in a chamber, such as by centrifugation, into at least one cellular portion and a primarily fluid portion; withdrawing the primarily fluid portion from the chamber; passing the primarily fluid portion back through the one separated cellular portion in the chamber at least once; and then removing the primarily fluid portion from the chamber thereby to effect a more complete separation of the primarily fluid portion from the one cellular portion of the blood.

Also according to the invention there is provided a method for fractionating a given amount of whole blood into components thereof and for collecting at least one cellular component, comprising the steps of supplying the whole blood to a first separation chamber mounted in a centrifuge device, centrifuging the whole blood in the first separation chamber and to cause fractionation fractionation of the whole blood into components thereof and to cause the components to congregate at different zones in the first separation chamber during centrifugation, withdrawing a first cellular com-

ponent of the blood from the separation chamber and recirculating that first component back through the first separation chamber with the whole blood until only the first component is being recirculated, withdrawing blood fluid containing plasma, and apssing that blood fluid back into the first separation chamber in a direction which traverses the flow path of whole blood into, and withdrawal of the first component from the first separation chamber in a predetermined number of times thereby to elute blood components other than the first cellular component from the whole blood and first component with the blood fluid and to wash the first component with the blood fluid.

Further according to the invention there is provided a system for automatically fractionating a given quantity of whole blood into components thereof and for collecting at least one component comprising: a centrifuge device, a first separation chamber mounted in said centrifuge device and having first and second inlets and first and second outlets, means for withdrawing whole blood from a source thereof and for supplying same to said first inlet of said first separation chamber, first conduit means for coupling said first outlet of said first separation chamber to the source for recirculation, fluid coupling means for coupling said second outlet of said first separation chamber to said second inlet of said first separation chamber and means for causing blood fluid to flow from said second outlet to said second inlet and through said first separation chamber, and said inlets and outlets of said first separation chamber being arranged so that blood fluid flowing in said first separation chamber from said second inlet to said second outlet traverses the flow path of whole blood entering said first inlet and the blood component exiting from said first outlet such that the flowing blood fluid elutes blood components from the whole blood while at the same time the flowing blood fluid washes the one component.

Still further according to the invention there is provided for use in a blood fractionating system wherein whole blood is passed into and through a separation chamber in a centrifuge device for fractionating the whole blood into components thereof, an improved separation chamber having four corners and adapted to be positioned in a diamond position so that the four corners define an upper corner, a lower corner, a first side corner and a second side corner, said upper corner having an outlet for blood fluid containing components being fractionated in said separation chamber, said lower corner having a re-entry inlet for blood fluid withdrawn from said upper corner, said first side corner having an inlet for the whole blood and said second side corner having an outlet for a blood component.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic fluid circuit diagram of the blood fractionating system of the present invention.

FIG. 2 is an enlarged perspective view of a portion of the centrifuge device utilized by the system 10 and shows the position of the separation chamber defined by plastic bags within the centrifuge device.

FIG. 3 is a top plan view of the plastic bags in the centrifuge device shown in FIG. 2.

FIG. 4 is a vertical elevational view of one side of the first separation chamber and is taken along line 4—4 of FIG. 3.

FIG. 5 is an edge view of the first separation chamber and is taken along line 5—5 of FIG. 4.

FIG. 6 is a vertical elevational view of a modified embodiment of the first separation chamber shown in the previous figures.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings in greater detail, there is illustrated schematically in FIG. 1, the system of the present invention, generally identified by reference numeral 10, for fractionating whole blood obtained from a banked or stored container or bag 12 of whole blood into the components of the blood, namely red blood cells, white blood cells, platelets and plasma.

The system 10 includes a centrifuge device 13 which is schematically represented by a disc 14 mounted for rotation on a shaft 16 having an axis of rotation 17. Further details of construction of the centrifuge device 13 can be found in co-pending applications (1) Ser. No. 843,222 entitled METHOD AND APPARATUS FOR PROCESSING BLOOD and (2) Ser. No. 843,296 entitled CENTRIFUGAL LIQUID PROCESSING SYSTEM, the disclosures of which are incorporated herein by reference. Mounted in the centrifuge device 13 is a first separation chamber 21, a second separation chamber 22 and a third separation chamber 23. As will be described in greater detail hereinafter, the first separation chamber 21 is the primary separation chamber where the whole blood is fractionated or separated into red blood cells and plasma containing white blood cells and platelets. The second separation chamber 22 is utilized for separating white blood cells from plasma by means of centrifugation and sedimentation. The third separation chamber 23 is utilized for separating platelets from plasma by means of centrifugation and sedimentation.

The system 10 further includes a plasma collection receptacle or bag 24 and a red blood cell collection receptacle or bag 26.

As shown, inlet and outlet fittings or connections 31 and 32 are provided in the whole blood bag 12. It is to be understood that, if desired, blood can be collected directly from a donor and processed by the system 10. One way of doing this is to have another fitting 33 in the whole blood bag 12. As shown, this fitting 33 is connected to a line which is connected to a donor. When collecting blood directly using the donor line and fitting 33, fitting 33 is open to allow blood to bleed into the bag 12. Also, the bag 12 initially is filled with an anticoagulant and fittings 31 and 32 are closed and have in-line cannulas which can be moved to open them.

To obtain a fresh supply of whole blood, the donor line is connected to a donor and a quantity of blood is bled into the bag 12. Then the donor line is cut and sealed such as by an R.F. heat sealing device. Then the in-line cannulas are moved to open fittings 31 and 32 and the whole blood in the bag 12 is ready to be processed.

As shown, the first separation chamber 21 has a generally square or diamond shape and is situated in a diamond position within the centrifuge device 13. Positioned in this manner, the first separation chamber 21 has a first side corner 34, an opposite second side corner 36, a lower corner 38, and an upper corner 40. As will be described in greater detail in connection with the description of FIG. 4, the corners 34–40 each have openings for receiving conduits, (e.g.) plastic tubings.

As indicated in FIG. 1 the second separation chamber has a lower inlet 42 and an upper outlet 44. The upper

outlet 44 is connected by a short conduit 46 to an upper inlet 48 of the third separation chamber 23 which also has an upper outlet 50.

The system 10 further includes a plurality of conduits defined below, which are typically flexible transparent plastic tubings. A first such conduit 52 couples the outlet 32 from the whole blood bag 12 to the first inlet at the first side corner 34 of the first separation chamber 21 and through a peristaltic pump 54. A portion 56 of conduit 52 is received in and forms part of the pump 54. A second conduit 58 is connected between a first outlet at the opposite side corner 36 of the first separation chamber 21 to the inlet 31 to the whold blood bag 12. Also, as shown, the second conduit 58 has a junction 60 therein and a third conduit 62 is connected to the junction 60 for the purpose of coupling the second conduit 58 to the red blood cell collection bag 26. A fourth conduit 64 is connected to a second outlet at the upper corner 40 of the first separation chamber 21 and extends out of the centrifuge device 13 and through a monitoring and sensing device 66 which is associated with a light transmitting portion 68 of the fourth conduit 64. Another portion 70 of the fourth conduit 64 passes over and forms part of a peristaltic pump 72. From there, the fourth conduit 64 extends back into the centrigude device to the lower inlet 42 of the second separation chamber 22. As explained above, the outlet 44 from the second separation chamber 22 is coupled by a short conduit 46 to the third separation chamber 23 and the outlet 50 thereof is coupled to a fifth conduit 74 which extends back out of the centrifuge device 13 and through a bubble trap 76. Then a portion 77 of the fifth conduit 74 extends over and forms part of another peristaltic pump 78 which is operated in tandem and in synchronization with the peristaltic pump 72. The fifth conduit 74 extends back into the centrifuge device to the second inlet at the lower corner 38 of the first separation chamber 21.

A sixth conduit 80 extends between a junction 82 in the fourth conduit 64 and the plasma collection bag 24. The junction 82 is located in the fourth conduit 64 between the portion 70 thereof and the inlet 42 to the second separation chamber 22.

It is to be understood that, if desired, the conduits 52 and 58 could be connected directly to a donor (as indicated by the phantom lines in FIG. 1) with, of course, safety devices in the conduits and a source of anticoagulant coupled to conduit 52 as explained in copending application Ser. No. 843,222 entitled METHOD AND APPARATUS FOR PROCESSING BLOOD.

Also, if desirable and as shown in FIG. 1, a source 90 of wash solution, such as saline solution, can be connected by a seventh conduit 92 to a junction 93 in the fifth conduit 74 between the portion 77 thereof and the bubble trap 76 and by an eighth conduit 94 to a junction 95 in the fourth conduit 64 between the portion 70 thereof and the junction 82.

In one preferred embodiment of the system 10 and as illustrated in FIG. 1, a source 96 of liquid, referred to herein as a storage medium, is coupled via a ninth conduit 98 to the fifth conduit 74 between junction 93 and pump 78. The storage medium is a liquid, e.g., water, containing dextrose and a saline solution. As will be explained in greater detail hereinafter the storage medium can be added to the red blood cells collected to add nutrients to them and give them more "body" or a "coating" to protect them from damage.

For controlling the various phases of operation of the blood fractionating system 10, the system 10 is provided with a plurality of valving devices which are realized by electromechanically controlled clamps associated with the conduits and which will be referred to hereinafter simply as valves. Each clamp, referred to herein as a valve, is situated on a piece of tubing for opening and closing fluid flow through the tubing and is not invasive of the closed system 10. These valves (clamps) are positioned as follows: A first valve 101 is associated with the second conduit 58 between junction 60 and inlet 31 to the whole blood bag 12. A second valve 102 is associated with the third conduit 62 between the junction 60 and the red blood cell collection bag 26. A third valve 103 is associated with the fourth conduit 64 between the junction 82 and the inlet 42 to the second separation chamber 22. A fourth valve 104 is associated with the fifth conduit 74 between the bubble trap 76 and the junction 93. A fifth valve 105 is associated with the sixth conduit 80 between the junction 82 and the plasma collection bag 24. A sixth valve 106 is associated with the seventh conduit 92 between the source 90 of wash solution and the junction 93 in the fifth conduit 74. A seventh valve 107 is associated with the eighth conduit 94 between the source 90 of wash solution and the junction 95 in the fourth conduit 64. And an eighth valve 108 is associated with the ninth conduit 98 between the storage medium source 96 and the fifth conduit 74.

Briefly summarizing the operation of the system 10, the processing of blood therein takes placed in a closed, aseptic environment. As shown, a supply of blood drawn from a donor or a previously banked supply of blood in the blood bag 12 is connected to the system 10. Then the pumps 54, 72 and 78 are operated with the pump 54 operating at roughly a fixed ratio of 3:1 to the speed of the pumps 72 and 78 which are operated in tandem. Whole blood is then pumped into the side corner 34 of the first separation chamber 21 which, by its configuration and orientation as will be described in greater detail in connection with the description of FIGS. 2–6, causes plasma, white blood cells and platelets to congregate at the upper corner 40 while red blood cells will congregate at the opposite side corner 36. The red blood cells congregating at the side corner 36 are caused to flow in the second conduit 58 by operation of the pump 54 to bring the red blood cells back into the whole blood bag 12. At this time, of course, first valve 101 is open and second valve 102 is closed. Meanwhile the centrifuge device 13 is rotating and the whole blood is being fractionated in the first separation chamber 21. The blood fluid, namely plasma containing white blood cells and platelets, at the upper corner 40 is withdrawn from the first separation chamber 21 by pump 72 and fed into the bottom of chamber 42. Also, of course, at this time valves 105,106,107 and 108 are closed and valves 103 and 104 are open.

Incidentally, the various conduits 52, 58, 64 and 74 that extend out of the centrifuge device are received through a larger tubing 110, a portion of which is shown by phantom lines. The larger tubing 110 is prevented from twisting while the centrifuge device 13 is rotating by means of rotating a holder for the tubing 110 at a different speed of rotation than the centrifuge device 13. This technique is explained in greater detail in co-pending application Ser. No. 843,222 entitled METHOD AND APPARATUS FOR PROCESSING BLOOD and obviates the need for fluid seals such that a completely closed system is obtained.

The pump 72 now pumps plasma with white blood cells and platelets through the conduit 64 and into the lower inlet 42 of the second separation chamber 22 which functions as a white blood cell separation chamber. Here, by means of the centrifugal force acting on the white blood cells and forcing them against the outer sidewall of the chamber 22, the white blood cells are separated from the platelets and sediment against the outer wall of the chamber 22 and the plasma flows out of the outlet 44 through the conduit 46 and into the platelet separation chamber 23. In this chamber 23 the platelets and plasma are caused to flow through a U-shaped path while undergoing centrifugation—the plasma flowing downwardly and then upwardly out the outlet 50. As a result of this flow path, the platelets are urged against the outer sidewall of the third separation chamber 23 and sediment out of the plasma. The plasma is then withdrawn through the fifth conduit 74 by means of the pump 78 and returned to the second inlet at the lower corner 38 of the first separation chamber 31.

As a result of the operation of the pumps 72 and 78, blood fluid rich in plasma and low in white blood cells and platelets flows across the first separation chamber 21 from the lower corner 38 to the upper corner 40 while whole blood flows across the first separation chamber 21 from the side corner 34 to the side corner 36. In this way, the plasma flow crossing the whole blood flow will elute the white blood cells and platelets from the whole blood and at the same time the plasma will wash the red blood cells. After this operation has taken place for a period of time, essentially only plasma is being passed vertically through the first separation chamber 21 and essentially only red blood cells are passed horizontally through the first separation chamber.

The fluid path for the plasma between the second outlet at the upper corner 40 and the second inlet at the lower corner 38 has a given volume and 3 to 8 of such volumes of plasma are circulated through the first separation chamber 21 during the processing of the given amount of whole blood in the blood bag 12. Preferably, 5 of these given volumes of plasma are passed through the first separation chamber 21 during processing of the given amount of whole blood. Also at the same time at least 3 volumes, e.g., pints, of whole blood are passed through the first separation chamber during processing of the given amount, e.g., pint of whole blood.

At this point in time the valve 103 will be closed and the valve 105 opened to collect plasma in the plasma collection bag. Then valve 101 is closed and valve 102 is opened to collect red blood cells.

Plasma is collected from conduit 64 after exiting from the upper corner of the separation chamber 21 and after having been recirculated through the first separation chamber 21 several times. However, plasma can be collected at a different point in the fluid circuit, e.g., after the plasma has passed through the three separation chambers 21, 22 and 23, by connecting the conduit 80 to the conduit 74 at the outlet side of pump 78. When connected in this manner, another valve (electromechanically operated clamp) is associated with the conduit 74 between the junction of the conduit 80 with the conduit 74 at the outlet side of the pump 78 and before the conduit 74 passes through the larger tubing 110. When it is desired to collect plasma, the additional valve is closed and valve 105 is opened. Although another valve is required, this arrangement may be desired for collecting plasma which has no, or a low incidence of, white blood cells and/or platelets therein.

If it is desired to further wash the red blood cells before collecting same after the plasma has been collected, valves 103, 104 and 105 can be closed and valves 106 and 107 opened so that a wash solution can be passed through the first separation chamber to wash the red blood cells which after being washed several times by the wash solution, can then be collected in the red blood cell collection bag 26.

Once the red blood cells are washed, they are in an unprotected state. Accordingly, it is often desirable to add fluid to the red blood cells when collecting them. This can be easily accomplished by adding back some platelet-poor plasma to the red cells by opening valve 105, maintaining valves 106 and 107 closed, and holding open valves 104 and 103.

Alternatively, fluid from the storage medium source containing dextrose, saline solution and nutrients can be added to the red blood cells to give them some "body" or a "coating", i.e., protection. This is accomplished by closing or maintaining closed valves 106 and 104 and opening valve 108 for a short time.

The blood fluid monitoring and sensing device 66 includes a light source 112 and a photodetector 114 which are arranged on either side of the light transmitting portion 68 of the conduit 64. Since it is desired not to mix red blood cells with the blood fluid containing plasma, white blood cells and platelets, the sensing device 66 is operable to sense the presence of red blood cells mixed with the blood fluid. When this occurs, suitable controls are operated to stop operation of the pumps 72 and 78 and to reverse operation of these pumps 72 and 78 for a predetermined period of time sufficient to return the RBC contaminated blood fluid (plasma) to the first separation chamber 21 for reseparation of the blood components. Then the control circuitry will reverse the operation of pumps 72 and 78 to cause them to pump in the original direction, namely the direction indicated in FIG. 1, to continue the operation of the system 10. Further details on the manner in which this may be accomplished are disclosed in copending application Ser. No. 843,222 entitled: METHOD AND APPARATUS FOR PROCESSING BLOOD.

Various methods for fractionating blood can be practiced utilizing the system 10 and a number of these methods are described below:

(1) In the simplest method for fractionating blood using the system 10, a given amount of whole blood is supplied to the separation chamber 21 followed by centrifuging the whole blood in the chamber 21 to cause the whole blood to separate into red blood cells at the side corner 36 and below with white blood cells above the red blood cells and plasma at the upper corner 40. Then the plasma with platelets and white blood cells is circulated through the separation chamber 21. In practicing this simple method for fractionating blood, the second and third separation chambers 22 and 23 can be omitted with the fourth and fifth conduits 64 and 74 being replaced by one fluid coupling for coupling the second outlet at the upper corner 40 through the peristaltic pumps 72 and 78 to the second inlet at the lower corner 38. Also in this method for fractionating a given amount of whole blood, the whole blood can be placed in the separation chamber 21 before operating the system 10 or can be supplied from the whole blood bag 12 and recirculated through the chamber 21 with eventu-

ally only red blood cells collecting at the corner **36** being recirculated. The passing of the plasma with platelets and white blood cells will effect a more complete separation of the red blood cells from the whole blood and the red blood cells can then be collected.

(2) Further method steps include the steps of collecting the plasma, platelets and white blood cells in the plasma collection receptacle **24** and then passing wash solution through the chamber **21** to wash the red blood cells which are being recirculated through the separation chamber **21** followed by collecting the red blood cells in either the whole blood bag **12** or the receptacle **26**.

(3) Still further method steps include the steps of returning the wash solution to the wash solution source **90** prior to collecting red blood cells and then adding a storage medium to the red blood cells when collecting the same.

(4) Another method includes the steps of supplying whole blood to the separation chamber **21**, centrifuging the blood in the separation chamber **21**, withdrawing plasma with some white blood cells and platelets from the chamber **21** and passing that plasma through the third chamber **23** to separate the platelets and white blood cells from the plasma by centrifugation and sedimentation in the third chamber **23** and then collecting the red blood cells with some white blood cells, the platelets with some white blood cells and the plasma with some white blood cells.

(5) A further step to this method defined in the previous paragraph (4) is to add wash solution prior to collecting red blood cells.

(6) A still further step to the method described in the last paragraph (5) is to add back some plasma to the red blood cells when collecting them to protect the red blood cells.

(7) An alternative step to the step described in the previous paragraph (6) is to add back some plasma to the red blood cells when collecting them.

(8) Still another method includes the steps for separating the red blood cells from the plasma and platelets and white blood cells as described in paragraph (1) above followed by passing the plasma with platelets and white blood cells through the second chamber **22** for separating white blood cells from the plasma and platelets and then collecting red blood cells with some plasma and some platelets, white blood cells and plasma with platelets.

(9) A further step to the method described in the previous paragraph (8) is to pass a wash solution through the chamber **21** after collecting the white blood cells and plasma with platelets to further wash the red blood cells.

(10) A still further step which can be added to the method described in the previous paragraph (9) is to add a nutrient or to add plasma with platelets to the red blood cells when collecting them after washing the red blood cells with the wash solution.

(11) A further, preferred method includes the steps of supplying a given amount of whole blood to the first separation chamber **21**, centrifuging the whole blood in the chamber **21** to cause fractionation of the whole blood into components thereof and to cause the components to congregate in different zones in the first chamber **21** during centrifugation, withdrawing the red blood cells from the first outlet at side corner **36** and recirculating them back through the first separation chamber **21** by reintroducing them into the first inlet at the side corner **34** with the whole blood until only red blood cells are being recirculated, withdrawing blood fluid, plasma containing platelets and white blood cells, from the upper corner **40** and passing that blood fluid containing plasma with white blood cells and platelets through the second separation chamber **22** to separate white blood cells from the blood fluid by centrifugation and sedimentation and then passing the blood fluid exiting from the second chamber **22** into the third chamber **23** to separate platelets from the blood fluid by centrifugation and sedimentation and passing the remaining blood fluid, namely plasma, back through the separation chamber **21** by introducing the plasma into the lower corner **38** of the chamber **21** and recirculating the plasma vertically through initially whole blood and later through just the red blood cells being recirculated horizontally through the chamber **21** to elute other particles from the red blood cells. After three volumes of the whole blood path have been circulated through chamber **21** and three to eight, preferably five, volumes of the plasma path have been recirculated through the separation chamber **21**, the red blood cells can then be collected in the receptacle **26** by closing valve **101** and opening valve **102** and plasma can be collected in receptacle **24** by closing valve **103** and opening valve **105**.

(12) An additional step to the method described in the previous paragraph (11) is to add back some of the plasma to the separation chamber **21** as the red blood cells are being collected in the receptacle **26**.

(13) A further step to add to the preceding step is to pass a wash solution through the chamber **21** before collecting red blood cells in the receptacle **26**.

(14) Another step to add to the method described in the previous paragraph (13) is to add back plasma to the red blood cells in chamber **21** after washing them with the wash solution and prior to completing collection of the red blood cells in the receptacle **26**.

(15) An alternative method step to the step described in the previous paragraph (14) is to add a storage medium instead of plasma to the red blood cells in the chamber **21** after they have been washed with the wash solution and prior to or during the collection of the red blood cells in the red blood cell collection receptacle **26**.

In the schematic diagram illustrated in FIG. **1** it is to be noted that the various containers, receptacles, chambers, etc. are shown in vertical positions which are directly related to the actual preferred vertical positions of these chambers or containers. In this respect, it will be apparent that the storage medium source **96** and wash solution source **90** are preferably located above the centrifuge device **13** to facilitate gravity flow of fluid from the source **96** and **90** into the centrifuge **13**.

It is to be understood that the various separation chambers **21**, **22** and **23** are defined by plastic bags which are held within specially formed platens (not shown). Platens and bags of this type are disclosed in co-pending application Ser. No. 843,296 entitled CENTRIFUGAL LIQUID PROCESSING SYSTEM. With this construction and arrangement of the chambers **21–23**, once the three plastic chamber-defining bags have been utilized for processing a pint of blood from a whole blood bag **12**, bag **21** can be discarded and bags **22** and **23** stored for future use of the white blood cells and platelets, and a new set of interconnected plastic bags and plastic tubings can be inserted into the system **10**, i.e., into the centrifuge device **13** thereof, for

again carrying out the method of blood fractionation in the system **10** as described above.

As best shown in FIG. **2** the plastic bags can take the shape of plastic bags having parallel spaced walls with the edges sealed together to form a seam running along the edge of the parallel spaced walls. In this respect, the first separation chamber **21** is defined by a plastic bag **121** having spaced sidewalls and a seam **125** extending around the bag **121** and between the sidewalls. The corners of the bag **121**, that is the corners **34, 36, 38** and **40** of the first separation chamber **21** defined by the bag **121**, have tubing connections **134, 136, 138** and **140** sealed in openings formed in the seam at the corners of the bag **121** and between the opposite sidewalls thereof.

The bag **121** has a diamond or square shape as described above and is positioned in platens (not shown) in a diamond position as shown.

The second separation chamber **22** is defined by a plastic bag **142** having spaced sidewalls and a seam **145** extending along the edges and a seam between the sidewalls extending along the edges of bag **142**. For convenience, the inlet **42** and outlet **44** are omitted from the view of bag **142** in FIGS. **2** and **3**. As shown, the bag **142** has a generally curved, rectangular shape and is positioned in the centrifuge device **13** in platens (not shown) on a cylindrical envelope coaxial with the axis **17** of rotation of the centrifugal device **13**.

In a similar manner, the third separation chamber **23** is defined by a plastic bag **153** which has spaced sidewalls and a seam **155** and which is received in and between platens (not shown) in the centrifuge device **13**. The bag **153** is similar to the bag **142** except that it is provided with some form of partition means that extends part way down from the top of the center of the bag **153** so that platelets and plasma are caused to follow a U-shaped path through the bag **153**. Again, for convenience, the inlet **48** and outlet **50** are omitted from FIGS. **2** and **3** and, as with bag **142**, the bag **153** has a curved, generally rectangular shape and is positioned in the centrifuge device **13** on a cylindrical envelope coaxial with the axis **17** of rotation of the centrifuge device and adjacent to the bag **142**.

As shown in FIGS. **2** and **3**, the first separation chamber **21**, bag **121**, is tilted inwardly toward the axis of rotation of the centrifuge device **13**. The angle of tilt can be from 0+ to 5 degrees. As best shown in FIG. **5**, the angle of tilt is preferably 1 degree. With the bag **121** positioned in this manner, the lower corner **38** of the chamber **21** defined by bag **121** is at a greater radius from the axis **17** than is the upper corner **40**. Also, and as best shown in FIG. **3**, the side corners **34** and **36** are located at approximately the same radius from the axis **17** of the centrifuge device **13**. In this way, when whole blood comes into the corner **34** the flow pushes the red blood cells to the side corner **36** and they are withdrawn therefrom. Then the plasma, which is lighter than the red blood cells will congregate at the shorter radius which is adjacent the upper corner **40** of the chamber **21**. Platelets will congregate below the plasma with white blood cells, (buffy coat), congregating between the platelets and the red blood cells. Plasma, platelets and white blood cells are withdrawn from the second outlet at the corner **40** and processed in the manner described above.

A modified embodiment of the first separation chamber **21** is shown in FIG. **6** and comprises a kite shaped plastic bag **221**. This modified kite shaped bag **221** has a generally kite shape with side corners thereof, **234** and **236**, located closer to the upper corner **240** than the bottom corner **238**. Also the side edges of the kite shaped bag **221** are curved. In this respect there are two upper curved edges **242** and **244**, and two lower curved edges **246** and **248**. These curved edges follow generally parabolic curves and the actual curves chosen are ones which follow the naturally occurring flow paths of the blood components as they are undergoing centrifugation within the bag **121** as it is tilted one degree from the vertical and toward the axis of rotation of the centrifuge device as described above. This bag provides a somewhat smoother flow of the blood components within the bag **221**. In this respect, with straight edges between corners, so-called "dead places" are found in the chambers where blood flow does not necessarily occur. This can be a problem when working with fresh blood since when flow does not occur there is a tendancy of the blood to clot and aggregate. Thus, elimination of "dead places" improves the efficiency of separation. Also the curved edge blood bag **221** reduces the volume of the separation chamber **221** without sacrificing performance of the system.

From the foregoing description it will be apparent that the system **10** of the present invention, the methods for utilizing the system **10** and the separation chamber **21** provide a number of advantages some of which have been described above and others of which are inherent in the invention. Also, it will be apparent to those skilled in the art that obvious modifications can be made to the system **10** and the bag **21** or **221** without departing from the teachings of the invention. Accordingly, the scope of the invention is only to be limited as necessitated by the accompanying claims.

We claim:

1. A method for fractionating a given amount of whole blood into several of its components, including the steps of: separating the whole blood in a chamber, such as by centrifugation, into at least one cellular portion and a primarily fluid portion; withdrawing the primarily fluid portion from the chamber; passing the primarily fluid portion back through the one separated cellular portion in the chamber at least once; and then removing the primarily fluid portion from the chamber thereby to effect a more complete separation of the primarily fluid portion from the one cellular portion of the blood.

2. The method according to claim **1** wherein said one cellular portion is comprised of red blood cells.

3. The method according to claim **1** wherein the fluid of said primarily fluid portion is comprised of plasma.

4. The method according to claim **1** wherein said primarily fluid portion is recirculated back through said one separated cellular portion by withdrawing said fluid portion from the top of the chamber containing said one cellular portion and introducing said fluid portion back into the bottom of the chamber.

5. The method according to claim **1** wherein said one cellular portion is comprised of red blood cells and said primarily fluid portion is comprised of plasma.

6. The method according to claim **1** wherein said one cellular portion is comprised of red blood cells and said primarily fluid portion is comprised of plasma and platelets.

7. The method according to claim **1** wherein said one cellular portion is comprised of red blood cells and said primarily fluid portion is comprised of plasma containing platelets and white blood cells.

8. The method according to claim 1 wherein said one cellular portion is comprised of red blood cells and wherein said method further includes the steps of: collecting the primarily fluid portion after passing it through the one cellular portion several times; passing a wash solution through the red blood cells; collecting the wash solution; and, then collecting the red blood cells.

9. The method according to claim 8 wherein some of said primarily fluid portion is added back to the red blood cells when collecting them.

10. The method according to claim 9 wherein said primarily fluid portion is comprised of plasma.

11. The method according to claim 8 wherein a storage medium containing nutrients is added to the red blood cells when collecting them.

12. The method according to claim 1 wherein said one cellular portion is comprised of red blood cells and said primarily fluid portion is comprised of plasma containing platelets and white blood cells and wherein said method further includes the steps of recirculating the primarily fluid portion through the red blood cells a predetermined number of times, collecting the primarily fluid component; and collecting the red blood cells.

13. The method according to claim 12 including the further steps of passing a wash solution through the red blood cells prior to collecting the red blood cells.

14. The method according to claim 13 including the step of adding a storage medium containing a nutrient to the red blood cells when collecting the red blood cells.

15. The method according to claim 1 wherein said one cellular portion is comprised of red blood cells and said primarily fluid portion is comprised of plasma containing platelets and white blood cells and wherein said method further includes the steps of: separating platelets from the primarily fluid portion, such as by passing the one fluid portion through a separation chamber undergoing centrifugation, prior to passing the primarily fluid portion back through the red blood cells; passing the platelet-poor primarily fluid portion through the red blood cells a predetermined number of times; collecting the plasma with some white blood cells; collecting the platelets with some white blood cells; and collecting the red blood cells with some white blood cells.

16. A method for fractionating a given amount of whole blood into components thereof and for collecting at least one cellular component, comprising the steps of supplying the whole blood to a first separation chamber mounted in a centrifuge device, centrifuging the whole blood in the first separation chamber to cause fractionation of the whole blood into components thereof and to cause the components to congregate at different zones in the first separation chamber during centrifugation, withdrawing a first cellular component of the blood from the separation chamber and recirculating that first component back through the first separation chamber with the whole blood until only the first component is being recirculated, withdrawing blood fluid containing plasma, and passing that blood fluid back into the first separation chamber in a direction which traverses the flow path of whole blood into, and withdrawal of the first component from the first separation chamber a predetermined number of times thereby to elute blood components other than the first cellular component from the whole blood and first component with the blood fluid and to wash the first component with the blood fluid.

17. The method according to claim 16 wherein the given amount of whole blood is contained in a closed container and said method is performed in a completely closed environment.

18. The method according to claim 16 wherein said given quantity of blood is initially taken from a donor and banked in a sealed air-tight bag from which it is supplied to the first separation chamber.

19. The method according to claim 18 including the step of collecting the first component comprised of red blood cells in the blood bag.

20. The method according to claim 18 including the step of collecting the first component comprised of red blood cells in a receptacle.

21. The method according to claim 20 including the step of recirculating the first blood component back through the whole blood bag for a predetermined period of time to ensure that all of the whole blood has been processed in and through the first separation chamber followed by collecting the first blood component comprised of red blood cells in the receptacle.

22. The method according to claim 16 including the steps of monitoring the compoistion of the blood fluid being withdrawn from the first separation chamber and adjusting the rate of supplying whole blood from a whole blood source in response to the composition sensed.

23. The method according to claim 16 including the steps of passing the blood fluid through a second separation chamber undergoing centrifugation to separate a second cellular blood component from the blood fluid prior to passing the blood fluid back through the first separation chamber; withdrawing the remaining blood fluid from the second separation chamber; and, then passing that blood fluid back into the first separation chamber.

24. The method according to claim 23 including the steps of monitoring the composition of the blood fluid being withdrawn from the first separation chamber and adjusting the rate of supplying whole blood from a whole blood source in response to the composition sensed.

25. The method according to claim 23 wherein the step of monitoring the composition of the blood fluid being withdrawn from the first separation chamber is for the purpose of sensing red blood cells mixed with the blood fluid and includes the steps of: stopping and then reversing for a predetermined time period the flow of blood fluid from the first separation chamber when red blood cells are sensed in the blood fluid thereby to return the mixture of blood fluid and red blood cells to the first separation chamber for reseparation of the blood components therein; adjusting the rate of supplying whole blood to the first separation chamber and the rate of withdrawal of blood fluid from the first separation chamber in response to the sensing of red blood cells in the blood fluid; and reversing the flow of blood fluid so that it is again withdrawn from the first separation chamber to continue the processing of the whole blood.

26. The method according to claim 25 wherein the sensing of the composition of blood fluid being withdrawn from the first separation chamber is performed outside of the centrifuge device.

27. The method according to claim 25 wherein the ratio of the rate of supplying whole blood to the first separation chamber is maintained at a given ratio.

28. The method according to claim 27 wherein the ratio of the rate of supplying whole blood to the first separation chamber to the rate of withdrawal of blood fluid from the first separation chamber is approximately 3:1.

29. The method according to claim 23 wherein said second cellular component is comprised of platelets.

30. The method according to claim 23 wherein said second cellular component is comprised of white blood cells.

31. The method according to claim 23 including the step of coupling a third separation chamber between the outlet from the second separation chamber and the inlet to the first separation chamber and wherein the first blood component separated from the whole blood in the first separation chamber constitutes red blood cells, the second component separated in the second separation chamber by centrifugation and sedimentation constitutes white blood cells and a third component which is separated by centrifugation and sedimentation in the third separation chamber constitutes platelets.

32. The method according to claim 31 including the step of collecting plasma in a plasma collection receptacle after the blood fluid containing plasma has been passed through the separation chambers for a predetermined period of time.

33. The method according to claim 32 including the step of passing the blood fluid exiting from the third separation chamber through a bubble trap prior to its re-entry into the first separation chamber.

34. The method according to claim 31 including the steps of: blocking the flow of blood fluid to the second separation chamber and the flow of blood fluid from the third separation chamber into the first separation chamber; coupling the outlet and inlet for the blood fluid from and into the first separation chamber to a source of wash solution; recirculating the first blood component back through the first separation chamber; passing the wash solution through the first separation chamber for a predetermined period of time to wash the first blood component constituting red blood cells and then collecting the red blood cells in a receptacle.

35. The method according to claim 34 including the step of adding some of the plasma to the red blood cells when collecting them.

36. The method according to claim 34 including the step of adding a storage medium to the red blood cells when collecting them.

37. The method according to claim 16 wherein the fluid path for the blood fluid has a given volume and 3 to 8 of such given volumes of blood fluid are circulated through the first separation chamber during the processing of the given amount of whole blood.

38. The method according to claim 37 wherein approximately 5 given volumes of blood fluid are passed through the first separation chamber during processing of the given amount of whole blood.

39. The method according to claim 16 wherein at least 3 given volumes of whole blood are passed through the first separation chamber during the processing of the given amount of whole blood.

40. A system for automatically fractionating a given quantity of whole blood into components thereof and for collecting at least one component comprising: a centrifuge device, a first separation chamber mounted in said centrifuge device and having first and second inlets and first and second outlets, means for withdrawing whole blood from a source thereof and for supplying same to said first inlet of said first separation chamber, first conduit means for coupling said first outlet of said first separation chamber to the source of recirculation, fluid coupling means for coupling said second outlet of said first separation chamber to said second inlet of said first separation chamber and means for causing blood fluid to flow from said second outlet to said second inlet and through said first separation chamber, and said inlets and outlets of said first separation chamber being arranged so that blood fluid flowing in said first separation chamber from said second inlet to said second outlet traverses the flow path of whole blood entering said first inlet and the blood component exiting from said first outlet such that the flowing blood fluid elutes blood components from the whole blood while at the same time the flowing blood fluid washes the one component.

41. The system according to claim 40 wherein said source of whole blood is a closed container and said system processes blood in a completely closed system.

42. The system according to claim 40 wherein said source of whole blood is a donor.

43. The system according to claim 40 wherein said source of whole blood is a container for whole blood and said system includes an inlet and an outlet connected to said container.

44. The system according to claim 43 wherein said container has another inlet for bleeding blood into said container from a donor after which the said another inlet is sealed.

45. The system according to claim 43 including a receptacle for collecting red blood cells, second conduit means for coupling a junction in said first conduit means to said receptacle, said outlet from said container being coupled to said first inlet of said first separation chamber, first valve means associated with a portion of said first conduit means between said junction and said container for controlling fluid flow in said first conduit means and second valve means associated with said second conduit means for controlling fluid flow in said second conduit means whereby the first blood component constituting red blood cells exiting from the first outlet of said first separation chamber first can, by operation of said first and second valve means, be caused to flow back through said container and back into said first separation chamber and subsequently can, by further operation of said first and second valve means, by delivered directly to said red blood cell collection receptacle.

46. The system according to claim 45 wherein said first and second conduit means are flexible tubings and said first and second valve means are electromechanically controlled clamps associated with said respective flexible tubings.

47. The system according to claim 40 including means associated with said fluid coupling means for monitoring and sensing the composition of the blood fluid being withdrawn from said first separation chamber and for causing a predetermined quantity of blood fluid to be returned to the first separation chamber when red blood cells mixed with the blood fluid are sensed.

48. The system according to claim 48 wherein a light transmitting portion of said fluid coupling means is situated outside said centrifuge device and said means for monitoring and sensing the composition of the blood fluid withdrawn from said first separation chamber includes a light source and a photodetector associated

with said light transmitting portion of said fluid coupling means.

49. The system according to claim 40 including a second separation chamber situated in said centrifuge device and having an inlet and an outlet and wherein said fluid coupling means includes second conduit means for coupling said second outlet of said first separation chamber to said inlet of said second separation chamber and third conduit means for coupling said outlet of said second separation chamber to said second inlet of said first separation chamber.

50. The system according to claim 49 including a third separation chamber coupled into said third conduit means in series with and between said outlet of said second separation chamber and said second inlet of said first separation chamber.

51. The system according to claim 50 wherein said third separation chamber is a platelet separation bag which has a curved, generally rectangular shape and which is positioned in said centrifugal device on a cylindrical envelope coaxial with the axis of rotation of said centrifuge device.

52. The system according to claim 49 including a bubble trap coupled into said third conduit means in series with and between said second separation chamber and said second inlet to said first separation chamber.

53. The system according to claim 49 including a plasma collection receptacle, fourth conduit means for coupling a junction in said second conduit means to said plasma collection receptacle, first valve means associated with said fourth conduit means between said junction and said plasma collection receptacle for controlling fluid flow in said fourth conduit means, and second valve means associated with said second conduit means for controlling fluid flow in said second conduit means and said second inlet to said second separation chamber, said second valve means being operable to block flow of plasma from said second outlet of said first separation chamber to said inlet of said second separation chamber and the connection of said fourth conduit means and the opening of said first valve means then permitting flow of plasma to said plasma collection receptacle.

54. The system according to claim 53 wherein said source of whole blood, said red blood cell collection receptacle and said plasma collection receptacle are situated outside said centrifuge device and said first, second and third conduit means comprise flexible tubings which extend from said centrifuge device and are rotated at a speed different than the speed of rotation of said centrifuge device to prevent twisting of the tubings thereby to provide a closed fluid system.

55. The system according to claim 53 wherein said conduit means comprise flexible tubings and each of said valve means comprises an electromechanically controlled clamp associated with one of said tubings.

56. The system according to claim 40 including a source of wash solution, second conduit means for coupling said source of wash solution to said fluid coupling means, first valve means associated with said fluid coupling means for blocking flow of blood fluid through said fluid coupling means and through said first chamber and second valve means associated with said second conduit means for permitting flow of wash solution through said second conduit means to said fluid coupling means and through said first separation chamber.

57. The system according to claim 56 including a source of storage medium, third conduit means for coupling said source of storage medium to said fluid coupling means and third valve means associated with said third conduit means to permit flow of storage medium through said third conduit means to said first separation chamber.

58. The system according to claim 57 wherein said conduit means and said fluid coupling means are comprised of flexible tubings and each of said valve means comprises an electromechanically controlled clamp associated with one of said tubings.

59. The system according to claim 49 including first valve means associated with said third conduit means between said second separation chamber and said inlet to said first separation chamber for controlling fluid flow in said third conduit means, a source of wash solution having a first fluid connection to said third conduit means between said first valve means and said second inlet to said first separation chamber and having a second fluid connection to said second conduit means, second valve means associated with said first fluid connection for controlling fluid flow through said first fluid connection, third valve means associated with said second fluid connection for controlling fluid flow therethrough, and fourth valve means associated with said second conduit means for controlling fluid flow therethrough and connected between said second fluid connection to said second conduit means and said inlet to said second separation chamber.

60. The system according to claim 59 including a source of storage medium, fourth conduit means for coupling said storage medium source to said third conduit means and fifth valve means associated with said fourth conduit means for controlling flow of storage medium through said fourth conduit means to said first separation chamber.

61. The system according to claim 60 wherein said conduit means and said fluid connections comprise flexible tubings and each of said valve means comprises an electromechanically controlled clamp associated with one of said tubings.

62. The system according to claim 49 wherein said second and third conduit means each have a portion thereof situated outside said centrifuge device and said blood fluid flow causing means includes first and second peristaltic pumps operated synchronously in tandem, said first pump being associated with and including said portion of said second conduit means and said second pump being associated with an including said portion of said third conduit means.

63. The system according to claim 62 wherein said conduit means comprises flexible tubings which extend out of said centrifuge device and which are rotated at a different speed of rotation than said centrifuge device to prevent twisting thereby to provide a closed fluid system.

64. The system according to claim 49 wherein said second separation chamber is a curved, generally rectangular, white blood cell collection bag which is located in said centrifuge device on a cylindrical envelope coaxial with the axis of rotation of said centrifuge device.

65. The system according to claim 40 wherein said first separation chamber has four corners and is arranged in a diamond position within said centrifuge device so as to have an upper corner, a lower corner, a first side corner, and a second side corner, said upper corner having said second outlet for blood fluid, said lower corner having said second inlet for re-entry of blood fluid into said first separation chamber, said first

side corner having said first inlet for whole blood and said second side corner having said first outlet for the one blood component.

66. The system according to claim 65 wherein said first separation chamber has spaced sidewalls which extend to each of said corners and has edges between said corners.

67. The system according to claim 66 wherein said first separation chamber is positioned in said centrifuge device with the radius from the axis of rotation of the centrifuge device to said upper corner being shorter than the radius from the axis of rotation of said centrifuge device to said lower corner.

68. The system according to claim 67 wherein said two side corners are each positioned respectively substantially the same radial distance from the axis of rotation of said centrifuge device.

69. The system according to claim 66 wherein said first separation chamber is positioned in the centrifuge device so that a plane extending between said upper and lower corners and including tangents at said corners is at an angle of between 0+ and 5 degrees to the vertical.

70. The system according to claim 69 wherein said angle is approximately 1 degree.

71. The system according to claim 65 wherein said first separation chamber has a generally square configuration.

72. The system according to claim 65 wherein said first separation chamber has a generally diamond configuration.

73. The system according to claim 65 wherein said first separation chamber has a general shape of a kite with said two side corners being closer to said upper corner than to said lower corner.

74. The system according to claim 73 wherein said edges of said first separation chamber extending between said corners thereof are concave.

75. The system according to claim 74 wherein said concave edges of said first separation chamber follow generally parabolic curves which are related to the parabolic flow paths of the blood components as they are being centrifuged in said first separation chamber.

76. For use in a blood fractionating system wherein whole blood is passed into and through a separation chamber in a centrifuge device for fractionating the whole blood into components thereof, an improved separation chamber having four corners and adapted to be positioned in a diamond position so that the four corners define an upper corner, a lower corner, a first side corner and a second side corner, said upper corner having an outlet for blood fluid containing components being fractionated in said separation chamber, said lower corner having a re-entry inlet for blood fluid withdrawn from said upper corner, said first side corner having an inlet for the whole blood and said second side corner having an outlet for a blood component.

77. The separation chamber according to claim 76 having spaced sidewalls which extend to each of said corners and edges between said corners.

78. The separation chamber according to claim 77 being adapted to be positioned in the centrifuge device with the radius from the axis of rotation of the centrifuge device to said upper corner being shorter than the radius from the axis of rotation of the centrifuge device to said lower corner.

79. The separation chamber according to claim 78 wherein said other two corners are each adapted to be positioned, respectively, at substantially the same radial distance from the axis of rotation of the centrifuge device.

80. The separation chamber according to claim 79 wherein said chamber is adapted to be positioned in the centrifuge device so that a plane extending between said upper and lower corners and including tangents at said corners is at an angle of between 0+ and 5 degrees to the vertical.

81. The separation chamber according to claim 80 wherein said angle is approximately 1 degree.

82. The separation chamber according to claim 76 having a generally square configuration.

83. The separation chamber according to claim 76 having a generally diamond configuration.

84. The separation chamber according to claim 76 having the general shape of a kite with said side two corners being closer to said upper corner than to said lower corner.

85. The separation chamber according to claim 84 wherein said edges of said separation chamber extending between said corners thereof are concave.

86. The separation chamber according to claim 85 wherein said concave edges of said chamber follow generally parabolic curves which are related to the parabolic flow paths of the blood components as they are being centrifuged in said chamber.

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[54] **APHERESIS APPARATUS AND METHOD**

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[52] **U.S. Cl.** **210/805**; 210/782; 210/789; 604/4; 604/5; 604/6; 494/37

[58] **Field of Search** 210/782, 789, 210/805; 604/4, 5, 6; 494/37

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,145,713	8/1964	Latham	604/4
3,957,197	5/1976	Sartory et al. .	
4,416,654	11/1983	Schoendorfer et al.	494/10
4,464,167	8/1984	Schoendorfer et al.	604/6
4,675,117	6/1987	Neumann et al.	210/789
4,990,132	2/1991	Unger et al.	604/6
5,141,645	8/1992	Shiraki et al.	210/513
5,370,802	12/1994	Brown	210/782

FOREIGN PATENT DOCUMENTS

0155684	3/1985	European Pat. Off. .	
WO87/06472	11/1987	WIPO .	

OTHER PUBLICATIONS

MCS Disposables, Users Manual for the Mobile Collection Systems, Haemonetics Corporation; pp. 4–1–4–5 (Jan., 1992).

Users Manual for Haeomonetics V50 Plus Apheresis System, pp. 1–4–1–6 (May, 1991).

Users Manual for Haemonetics V50 Plus Apheresis System—Extended Storage Platelets (ESP) Protocol Non–Time Saver, pp. 1–3, (May, 1991).

Schoendorfer et al., "The Surge Technique: A Method to Increase Purity of Platelet Concentrates Obtained by Centrifugal Apheresis," Transfusion 23: 182–189 (1983).

Smit Sibinga, Study Reports on Blood: "Fluid Dynamics in a Bowl," Haemonetics, (Apr., 1991).

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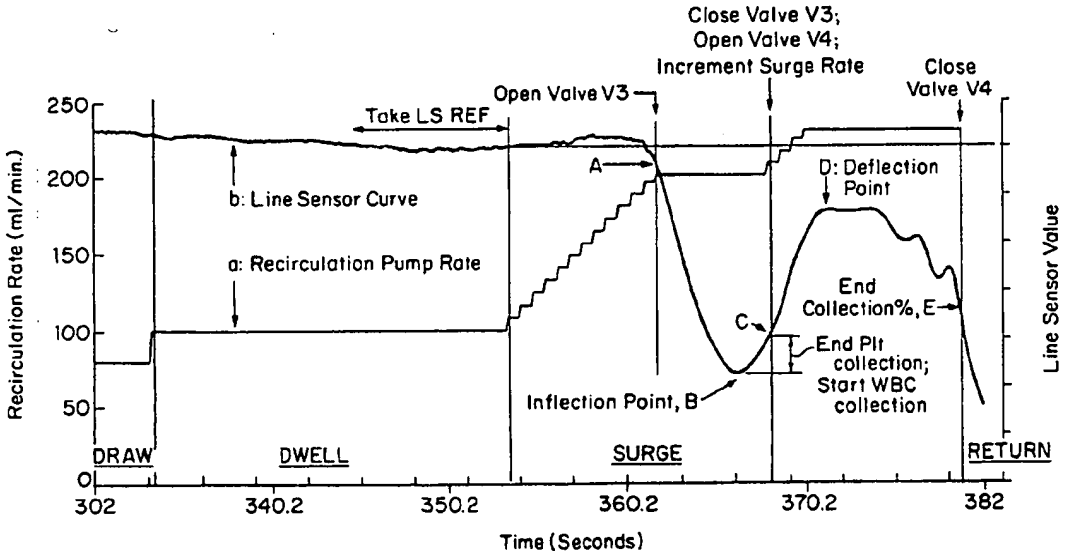
[57] **ABSTRACT**

An apheresis apparatus and method is disclosed for increasing the purity and yield of platelets separated from donated whole blood in a centrifuge. The whole blood in the centrifuge is diluted by recirculating fluid, such as plasma or saline, at a first flow rate, to mix with further withdrawn whole blood prior to entering the centrifuge. As plasma is collected, it is recirculated through the centrifuge at a second flow rate to further improve the separation between the intermediate density components, i.e., platelets and white blood cells in the "buffy coat." The plasma is then recirculated through the centrifuge at a third flow rate and platelets are displaced out of the centrifuge while the plasma is recirculating through the centrifuge at the third flow rate.

30 Claims, 11 Drawing Sheets



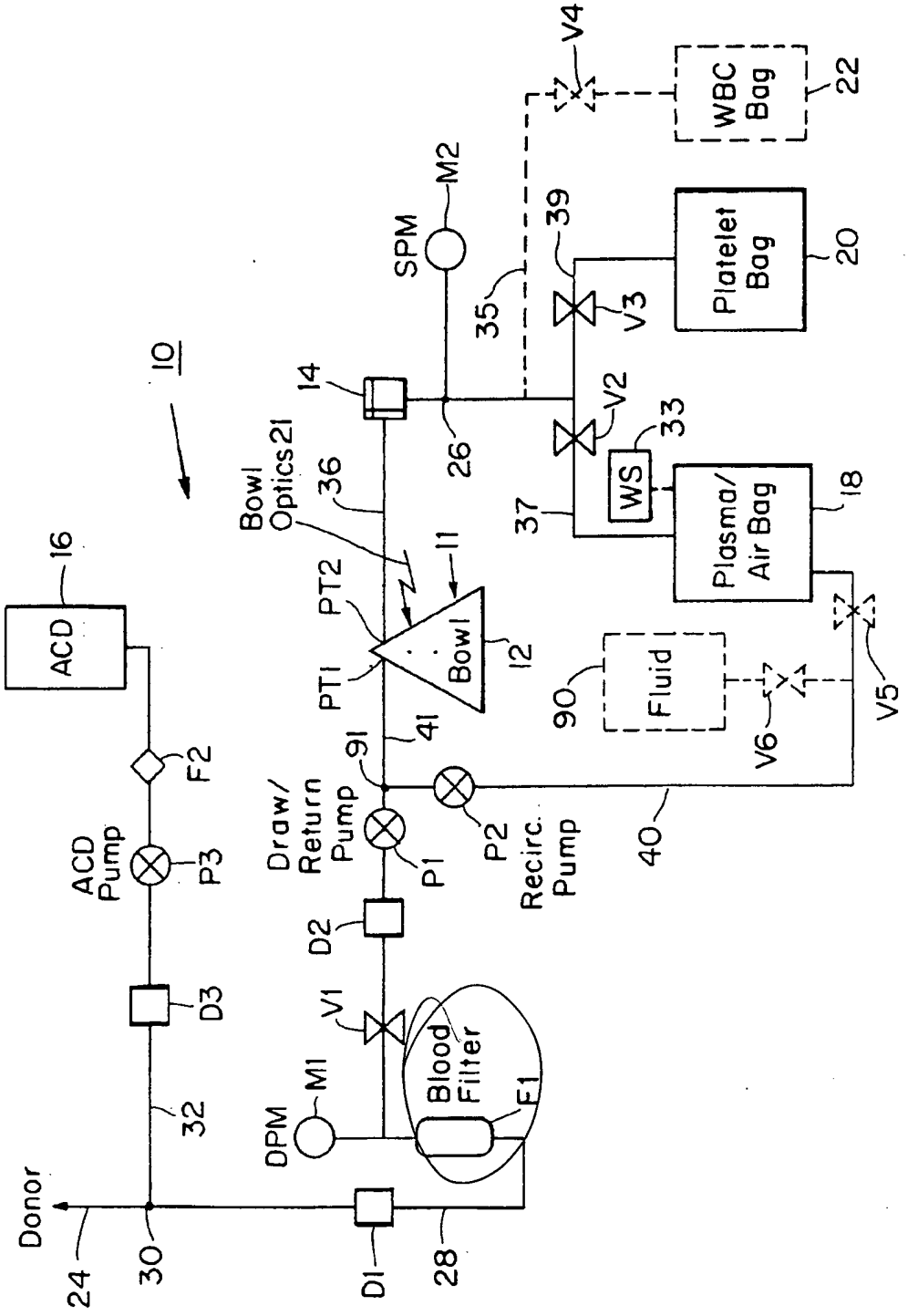

10
ACD
16
F2
ACD Pump
P3
D3
32
Donor
24
30
D1
28
DPM
M1
V1
Blood Filter
F1
D2
Draw/ Return Pump
P1
P2
Recirc. Pump
40
91
41
PT1
PT2
Bowl
12
11
Bowl Optics
21
36
14
SPM
M2
26
V4
WBC Bag
22
35
39
V3
Platelet Bag
20
V2
33
WS
37
Plasma/ Air Bag
18
90
Fluid
V6
V5

FIG. 1A

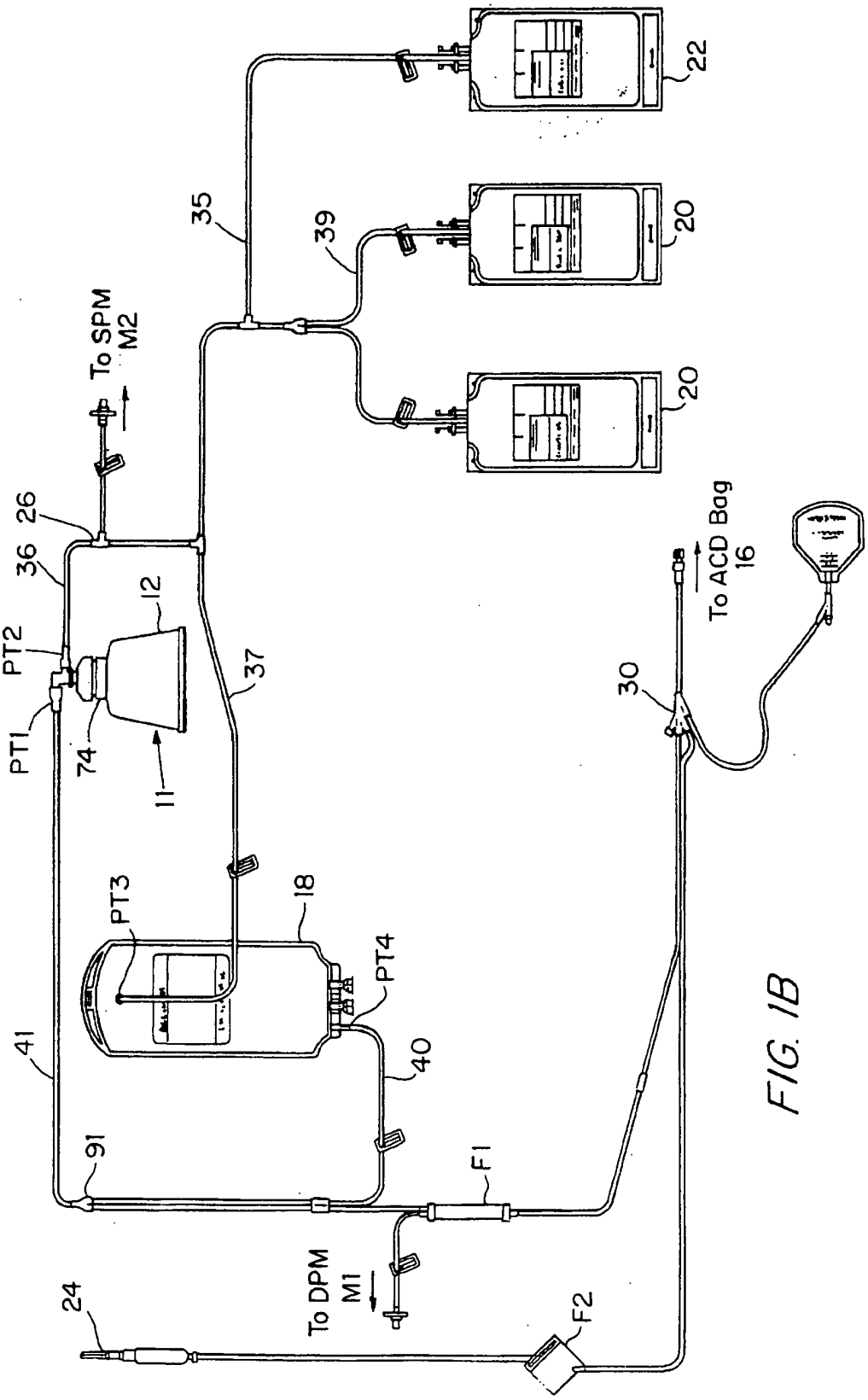

22
20
20
35
39
To SPM
M2
26
36
12
PT2
PT1
74
11
37
To ACD Bag
16
30
PT3
18
PT4
41
40
91
F1
To DPM
M1
24
F2

FIG. 1B

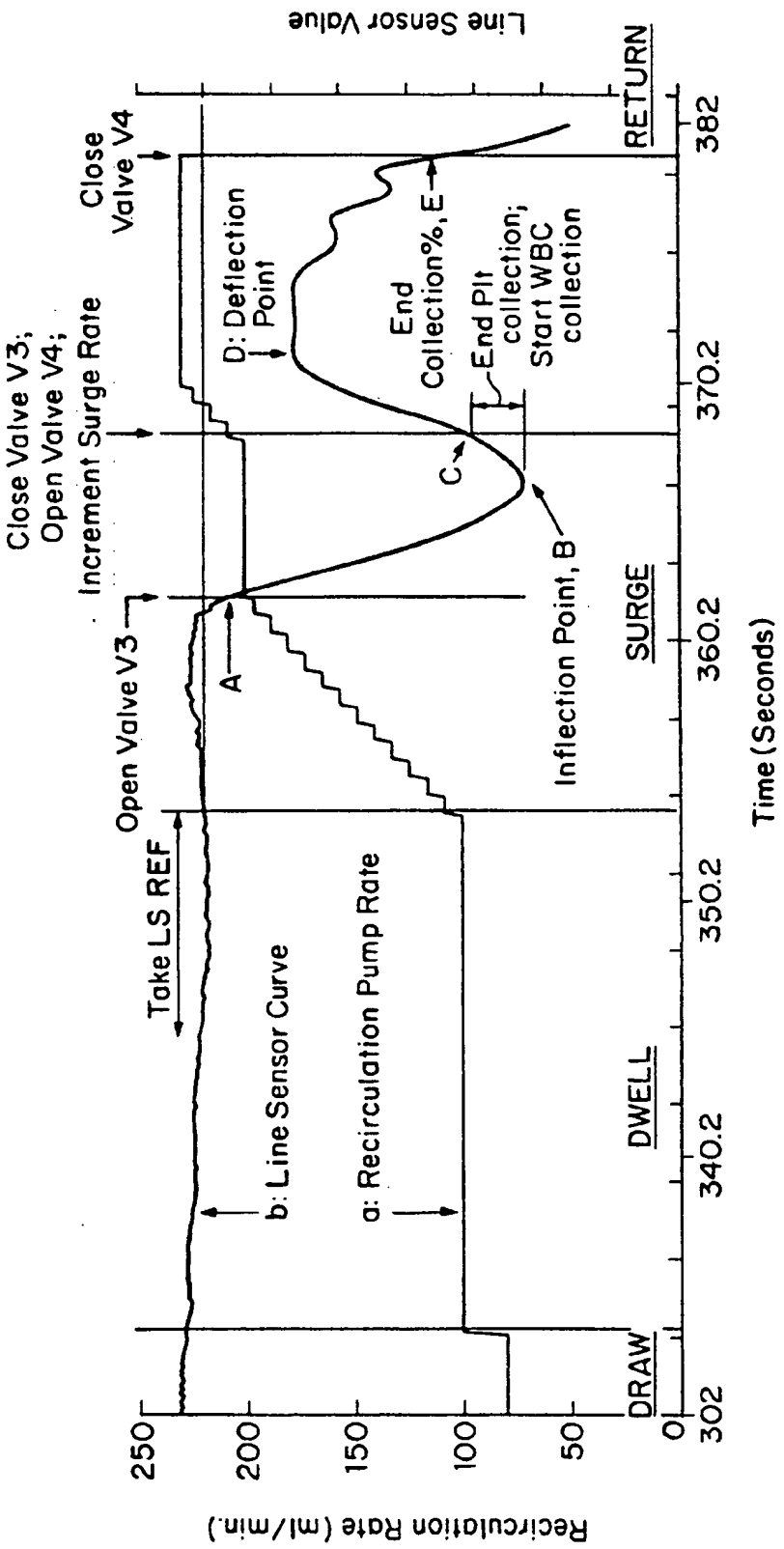

Line Sensor Value
RETURN
382
370.2
360.2
350.2
340.2
302
0
DRAW
DWELL
SURGE
Close Valve V4
D: Deflection Point
End Collection%, E
End Plt collection; Start WBC collection
C
Close Valve V3; Open Valve V4; Increment Surge Rate
Open Valve V3
A
Inflection Point, B
Take LS REF
b: Line Sensor Curve
a: Recirculation Pump Rate
250
200
150
100
50
Recirculation Rate (ml/min.)
Time (Seconds)

FIG. 2

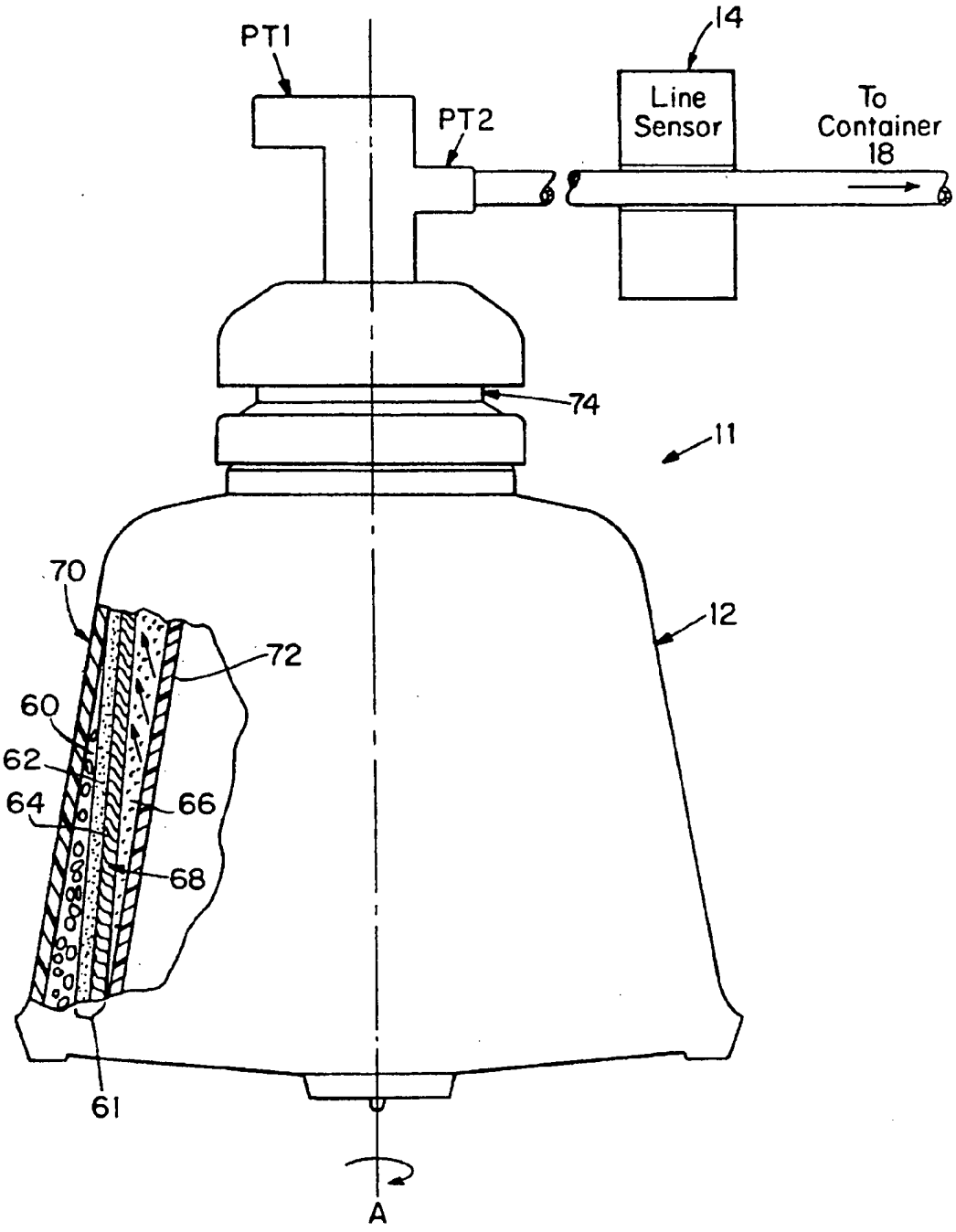

PT1
PT2
14
Line Sensor
To Container 18
74
11
12
70
72
60
62
64
66
68
61
A

FIG. 3

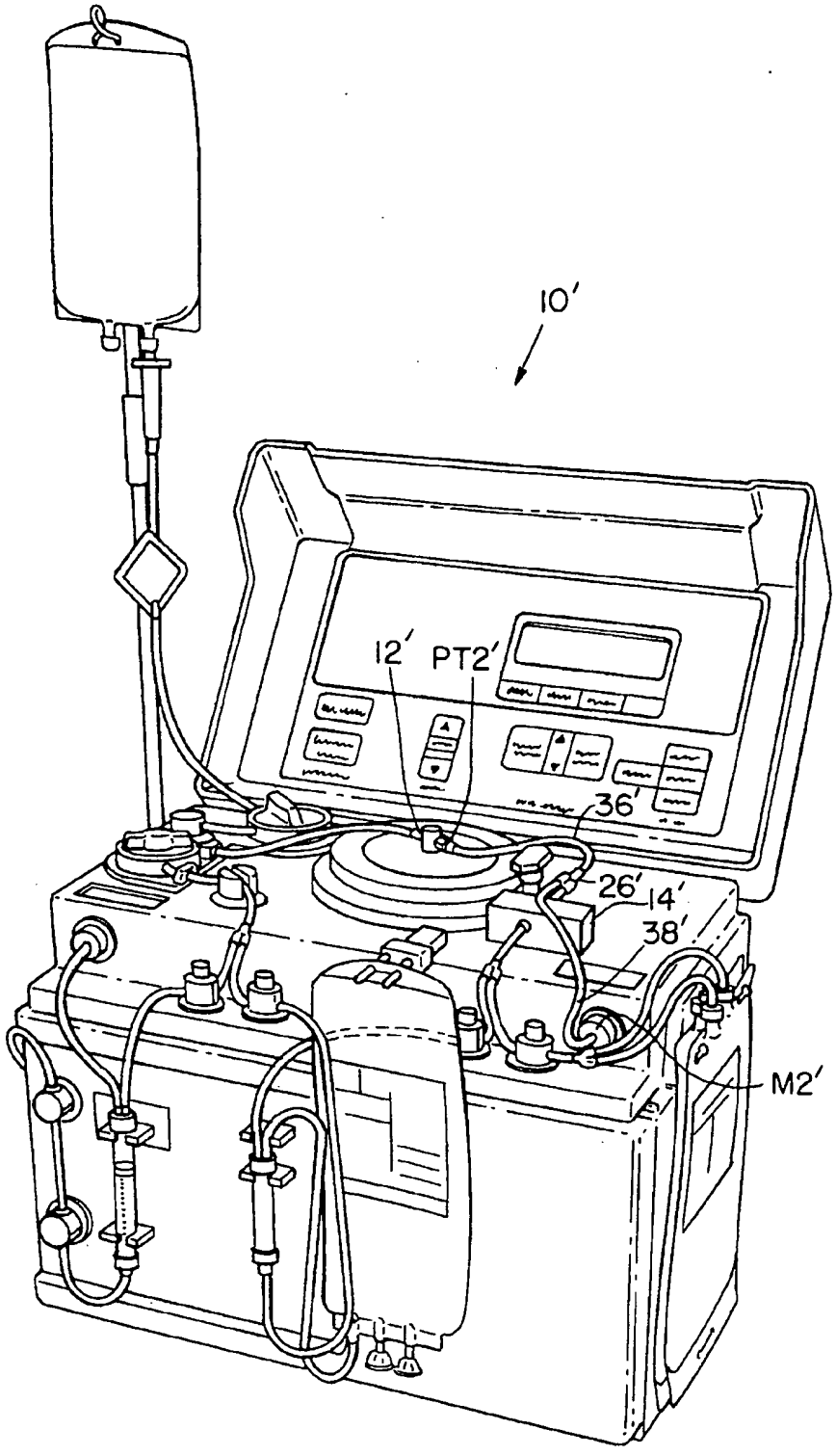


FIG. 4
PRIOR ART

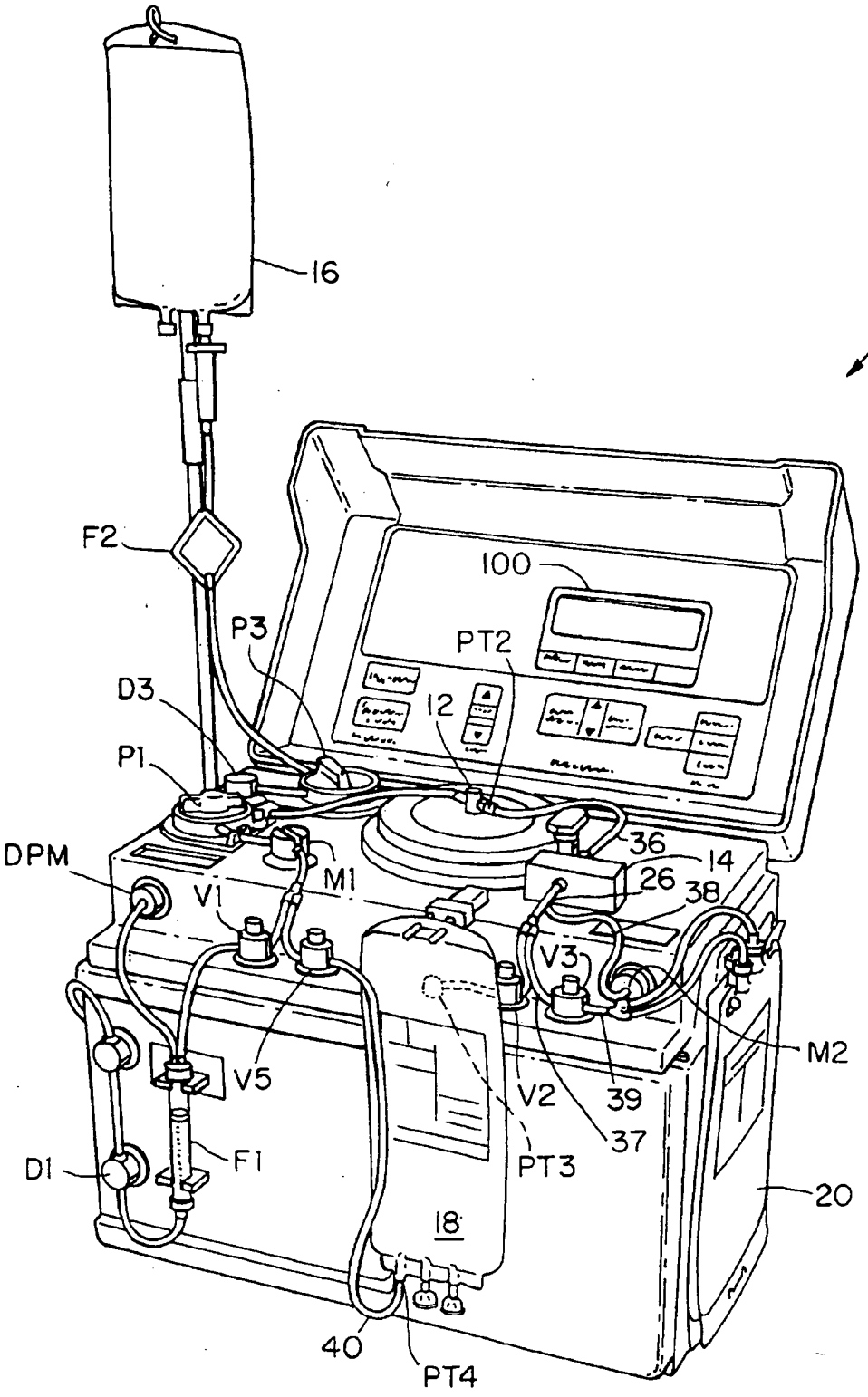

16
10
F2
100
P3
PT2
D3
12
P1
36
14
DPM
M1
26
38
V1
V3
M2
V5
V2
39
37
PT3
D1
F1
20
18
40
PT4

FIG. 5

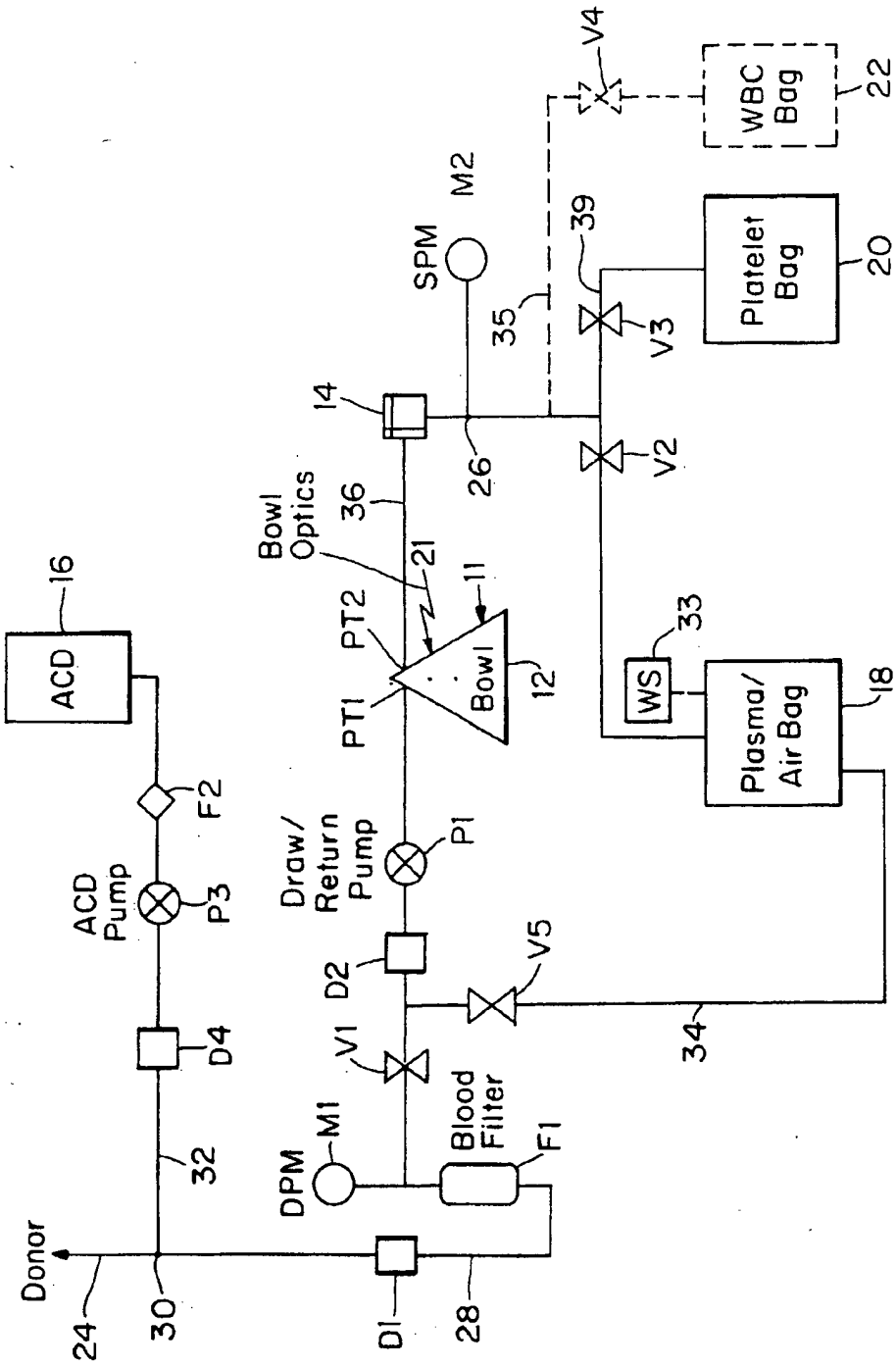

ACD
16
F2
ACD Pump
P3
D4
32
Donor
24
30
Draw/ Return Pump
P1
D2
V1
DPM
M1
Blood Filter
F1
D1
28
Bowl Optics
36
21
PT2
PT1
11
Bowl
12
14
26
SPM
M2
35
39
V4
WBC Bag
22
V3
Platelet Bag
20
V2
WS
33
Plasma/ Air Bag
18
V5
34

FIG. 6

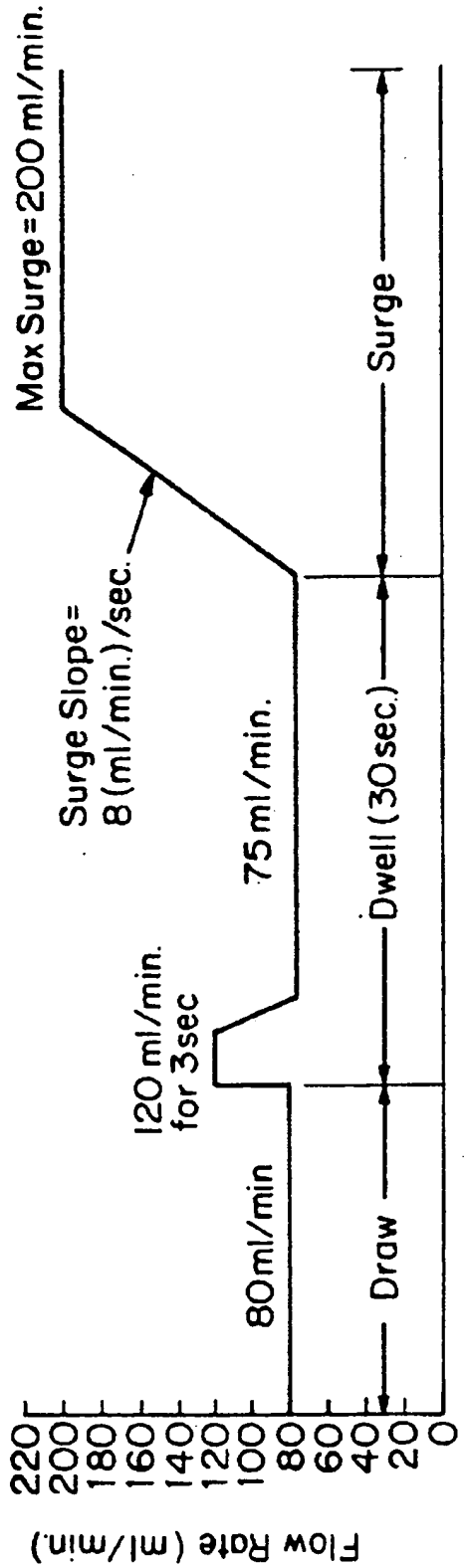

Max Surge=200 ml/min.
Surge Slope=
8 (ml/min.)/sec.
75 ml/min.
120 ml/min.
for 3sec
80ml/min
Surge
Dwell (30sec.)
Draw
Time
Flow Rate (ml/min.)
220
200
180
160
140
120
100
80
60
40
20
0

FIG. 7

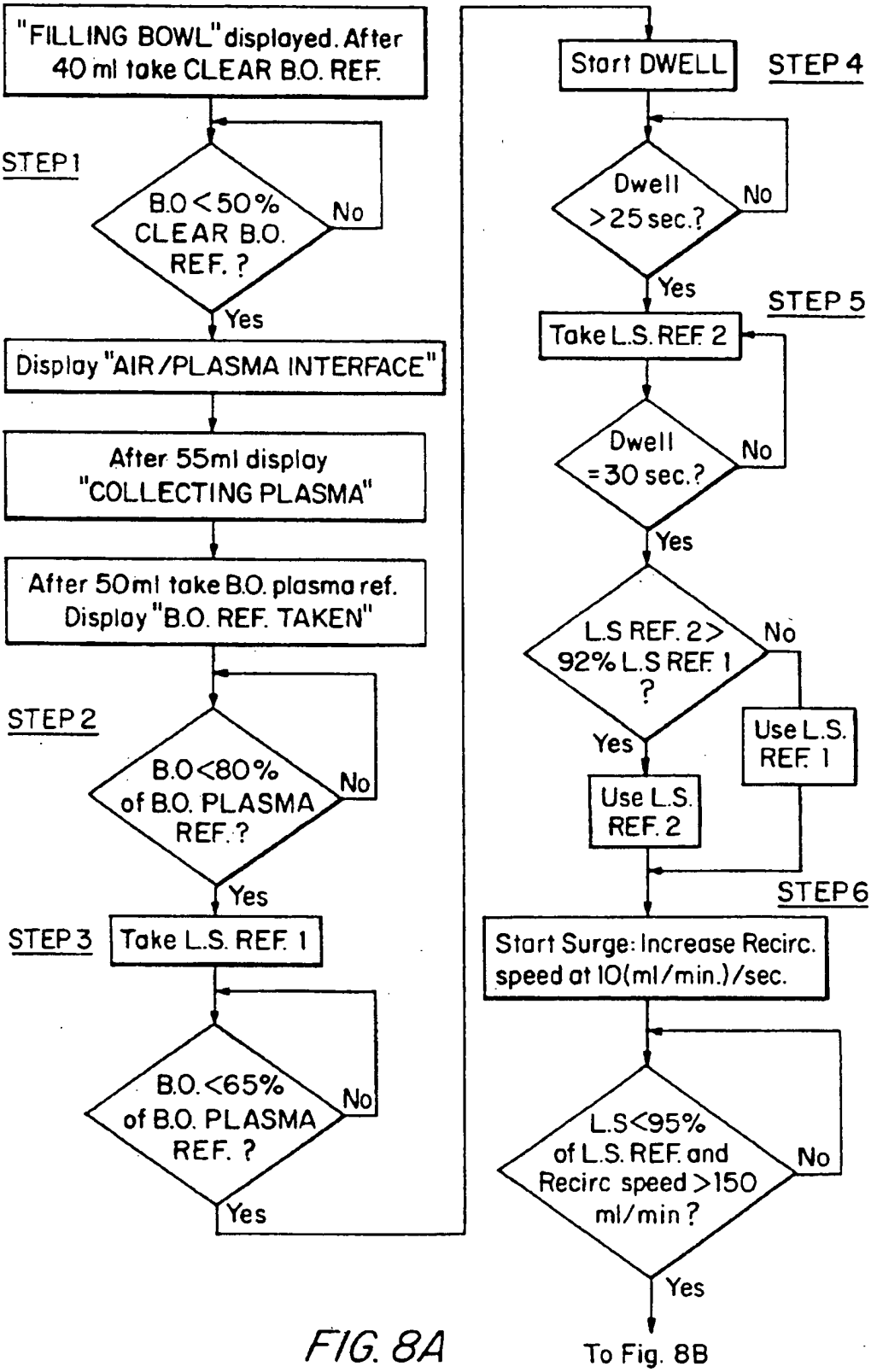

"FILLING BOWL" displayed. After 40 ml take CLEAR B.O. REF.
STEP 1
B.O < 50% CLEAR B.O. REF. ?
No
Yes
Display "AIR/PLASMA INTERFACE"
After 55ml display "COLLECTING PLASMA"
After 50ml take B.O. plasma ref. Display "B.O. REF. TAKEN"
STEP 2
B.O < 80% of B.O. PLASMA REF. ?
No
Yes
STEP 3
Take L.S. REF. 1
B.O. < 65% of B.O. PLASMA REF. ?
No
Yes
Start DWELL
STEP 4
Dwell > 25 sec.?
No
Yes
STEP 5
Take L.S. REF. 2
Dwell = 30 sec.?
No
Yes
L.S REF. 2 > 92% L.S REF. 1 ?
No
Yes
Use L.S. REF. 1
Use L.S. REF. 2
STEP 6
Start Surge: Increase Recirc. speed at 10(ml/min.)/sec.
L.S < 95% of L.S. REF. and Recirc speed > 150 ml/min ?
No
Yes
To Fig. 8B

FIG. 8A

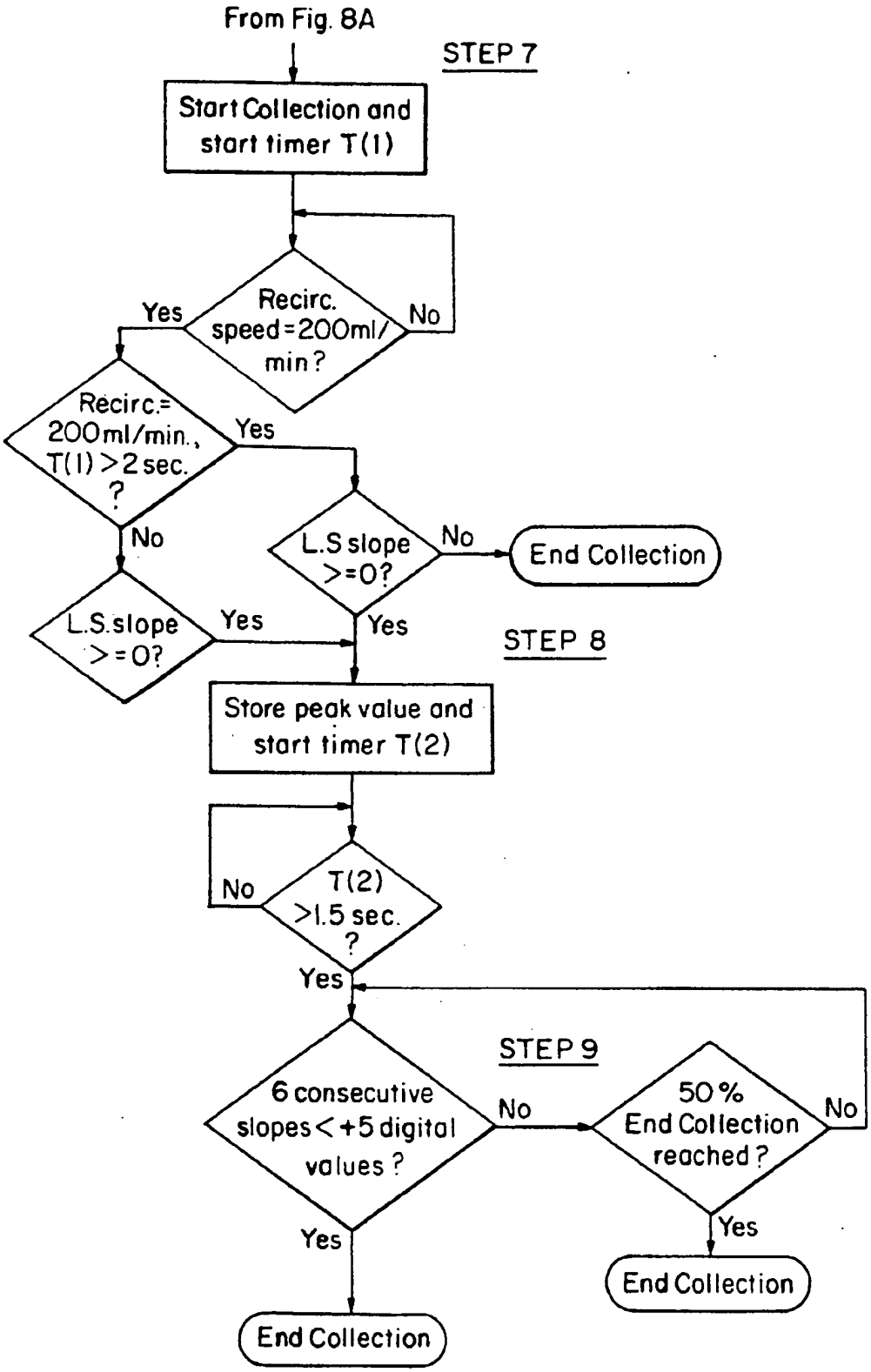

From Fig. 8A
STEP 7
Start Collection and start timer T(1)
Recirc. speed=200ml/min?
Yes
No
Recirc.=200ml/min., T(1)>2sec.?
Yes
No
L.S slope >=0?
No
End Collection
L.S.slope >=0?
Yes
Yes
STEP 8
Store peak value and start timer T(2)
T(2) >1.5 sec.?
No
Yes
STEP 9
6 consecutive slopes<+5 digital values?
No
50% End Collection reached?
No
Yes
End Collection
Yes
End Collection

FIG. 8B

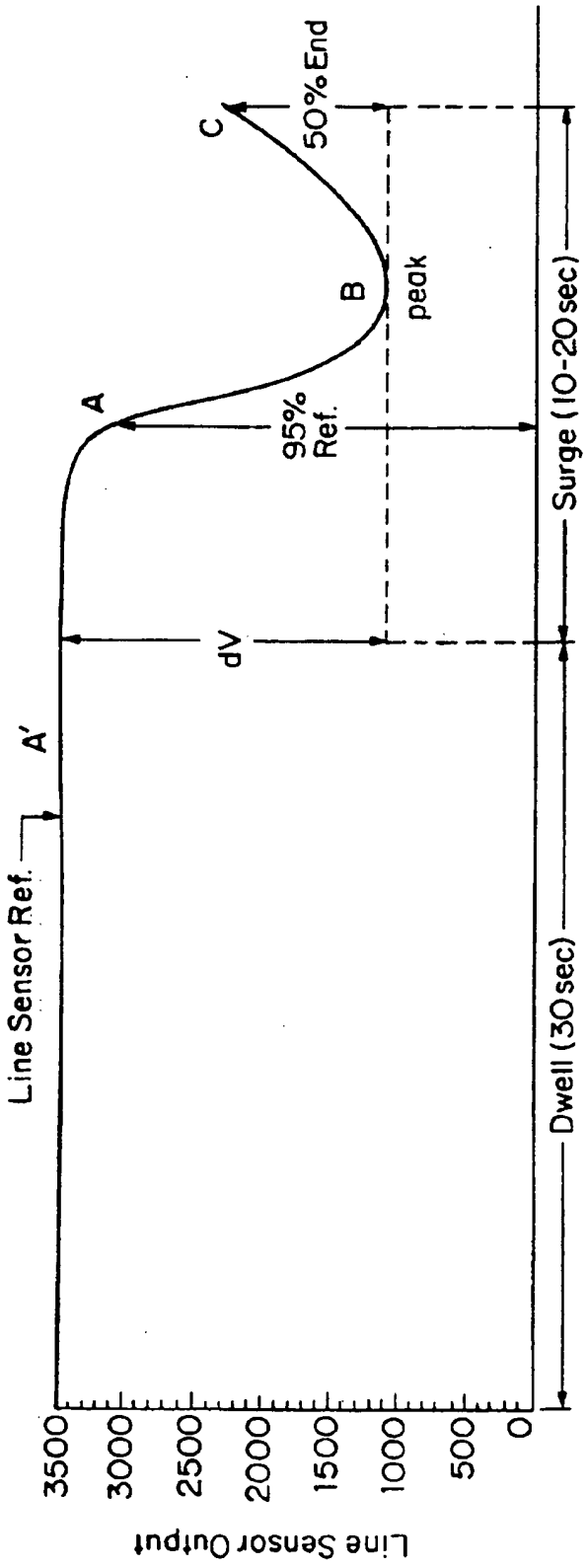

Line Sensor Output
3500
3000
2500
2000
1500
1000
500
0
Line Sensor Ref.
A'
A
B
C
dV
95% Ref.
50% End
peak
Surge (10-20 sec)
Dwell (30 sec)
Time

FIG. 9

APHERESIS APPARATUS AND METHOD

This application is a continuation of U.S. patent application Ser. No. 08/053,734 filed Apr. 27, 1993, which is abandoned.

BACKGROUND OF THE INVENTION

With the advance Of medical science, the demand for platelet concentrates with low contamination of white blood cells (WBC), such as, lymphocytes is rapidly growing. Platelets are fragments of a large cell located in the marrow called a megakaryocyte. Platelets have no nucleus and are primarily responsible for hemostasis, although they also have a role in tissue healing. They interact to chemicals released from damaged endothelial cells by becoming "sticky" and adhering to the damaged tissue. Platelets then release ADP, a chemical, which causes other platelets to stick to each other. This action, also known as aggregation, forms the primary white clot. Platelets then activate plasma proteins responsible for clotting which produce the "red" clot or the stable clot. Platelets have a half-life of 4–6 days in the normal adult. Normal platelet counts are 150,000–400,000/mm^3 in the adult. Platelet counts under 20,000/mm^3 can result in spontaneous bleeding.

With the improvement in cancer therapy patients are requiring increased platelet support. In addition, with the large number of screening tests employed for blood products, the number of units that are acceptable are less than in past years. The donor pool is reduced and therefore, the supply of random donor platelets must be conserved.

Procedures for collection of specific blood components from a single blood donor, apheresis, is proven to be a satisfactory approach to cover the demand for blood components. Recently, the equipment for collection of platelets has been directed towards maximizing the yield of pure platelets. (See for example, U.S. Pat. No. 4,416,654.) Today, it is understood that the contamination of platelet concentrates by WBC can lead to medical complications, such as graft-versus-host reactions.

Current blood separation equipment for the collection of platelet concentrates are not sufficient for automatically collecting an optimum pure platelet concentrate.

Accordingly, there is a continuing need for an apheresis separation apparatus and method for automatically collecting platelet concentrates with low white blood cell contamination while maximizing platelet yields.

SUMMARY OF THE INVENTION

The present invention provides a pheresis apparatus and method for increasing blood component yield from donated whole blood in a centrifugation fractionation volume. In accordance with the invention, whole blood is diluted by recirculating lower density fluid, preferably plasma, at a first flow rate, to mix with further withdrawn whole blood prior to entering the centrifuge. The diluted whole blood enters the fractionation or separation volume through an inlet port and is separated by centrifugation in the volume into a lower density components and higher density components. The higher density components are mainly red blood cells, white blood cells and platelets. The lower density component is mainly plasma.

During separation, lower density component is displaced from the volume through an outlet port to a first container. The blood pump is stopped and the collected lower density component is then returned to the separation volume through the inlet port at a second flow rate. The second flow rate is greater than the first flow through a "buffy coat" (made up of white blood cells and platelets), thereby diluting and widening the "buffy coat". The widened "buffy coat" improves the separation between white blood cells and platelets by allowing the denser white blood cells to sediment from the lighter platelets more completely to the outer layers of the buffy coat. In this manner, the separation of the higher density components remaining in the volume is improved. The improved separation between the white blood cells and platelets reduces the amount of white blood cell contamination when the platelets are finally collected.

The lower density component is then recirculated again through the volume at a third flow rate and component with density between lower density component and higher density components (the platelets) are displaced out of the volume while the lower density component is recirculating through the volume at the third flow rate. The third flow rate is at a rate greater than the second flow rate.

Blood components displaced from the volume are monitored by an optical line sensor which determines the specific component being displaced by the optical density of the component. An uninterrupted conduit or passageway is in fluid communication with the outlet port and extends from the outlet port beyond the optical line sensor. The optical line sensor is positioned intermediate the outlet port of the volume and the first container for collecting low density component.

An uninterrupted passageway prevents foam accompanying components displaced from the volume from being mixed more thoroughly with the components, thereby preventing false optical readings by the optical line sensor.

The present invention provides an apheresis apparatus and method for collecting platelet concentrates with lower white blood cell contamination than with existing apparatus and methods while maximizing platelet yields. The lower white blood cell contamination decreases exposure to viruses and possible alloimmunization.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the invention.

FIG. **1A** is a schematic drawing of a preferred embodiment of the apparatus of the present invention.

FIG. **1B** is a schematic drawing of a disposable system for use with the apparatus of FIG. **1A**.

FIG. **2** is a graph showing recirculation pump speed in ml/min (curve a) and line sensor output values (curve b) at different stages of the blood separation process for a three pump apparatus of FIGS. **1A** and **1B** of the invention.

FIG. **3** is a side view of a centrifuge bowl with a section broken away and connected to an optical line sensor **14**.

FIG. **4** is a plan view of a prior art apheresis apparatus showing a Y-connector upstream of the optical sensor **14**.

FIG. **5** is a plan view of the present invention showing a T-connector downstream of the optical sensor **14**.

FIG. **6** is a schematic drawing of a two pump preferred embodiment of the present invention.

FIG. 7 is a graph Showing pump speeds at different stages of blood separation for a two pump apparatus of the invention.

FIGS. 8A and 8B are a processing flow chart of a protocol for a 3-pump embodiment of the invention.

FIG. 9 is a graph showing the output of the line sensor in relation to time during the platelet collection process.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to FIGS. 1A and 1B, an apheresis system **10** uses a standard Latham type centrifuge **11** similar to the centrifuge described in U.S. Pat. No. 3,145,713 (incorporated herein by reference) for separating anticoagulated whole blood into its constituent components. The centrifuge **11** consists of a rotatable bowl **12** and stationary input and output ports PT1 and PT2 fluidly coupled to the bowl interior by a rotary seal **74** (see FIG. 3). An input port PT1 of centrifuge **11** is in fluid communication with phlebotomy needle **24** via blood filter F1, tubing **28** and Y-connector **30** when valve V1 is open. Tubing **28** is formed of blood compatible tubing as is all the tubing in apparatus **10**. An outlet port PT2 of centrifuge **11** is selectively coupled by valve V2 and tubing **36, 37** with a first container **18** labelled plasma/air bag suspended from weight scale **33**. A second container **20** labelled platelet bag is selectively coupled via valve V3 and tubing **39, 36** to outlet port PT2.

A third container **16** for storing anticoagulant, is in fluid communication with phlebotomy needle **24** via filter F2, tubing **32** and Y-connector **30**. Bacterial filter F2 prevents any bacteria in the anticoagulant (ACD) container **16** from entering the system. Containers **16, 18** and **20** are preferably plastic bags made of blood compatible material. Peristaltic pumps P1, P2 and P3, together with valves V1, V2 and V3, control the direction and duration of flow through apparatus **10** in response to signals generated, by line sensor **14**, donor pressure monitor (DPM) M1, system pressure monitor (SPM) M2 and air detectors D1, D2 and D3. Air detectors D1, D2 and D3 detect the absence or presence of fluid. Pressure monitors M1 and M2 monitor pressure levels within apparatus **10**. Line sensor **14** is an optical sensor which detects the presence of blood components passing through line sensor **14** from output port PT2.

In initial operation, pumps P1 and P3 are energized to prime tubing **28** of apparatus **10** with anticoagulant from container **16**. The anticoagulant passes through filter F2 and Y-connector **30** before reaching air detector D1. Air detector D1 senses the presence of anticoagulant at D1 and terminates the anticoagulant priming operation. During the priming operation, valve V2 is open and sterile air displaced from bowl **12** by the anticoagulant enters the top port PT3 of air/plasma container **18**.

Phlebotomy needle **24** is then inserted into the donor and the DRAW stage is commenced. The DRAW stage is the first stage in a sequence of 4 stages; DRAW, DWELL, SURGE and RETURN (see FIG. 2) performed by apparatus **10** when separating blood components. The pump speed for recirculation pump P2 during the DRAW, DWELL, and SURGE stages is graphically shown in curve a of FIG. **2**. During DRAW, whole blood is drawn from the donor at a rate of about 80 ml/min and mixed with anticoagulant using pumps P1 and P3. Pump P3 mixes anticoagulant from container **16** with the whole blood drawn from the donor. Valve V1 is open allowing anticoagulated whole blood to pass through tubing **28** and blood filter F1 before being pumped into bowl **12** through inlet port PT1. The whole blood is coupled to the bottom of the bowl **12** through a feed tube (not shown). The ratio of the anticoagulant to whole blood is typically about 1:10.

Referring to FIG. **3**., centrifuge **11** has a fixed inlet port PT1 and a fixed outlet port PT2. A rotary seal **74** fluidly couples the stationary inlet port PT1 to the lower interior portion of the bowl **12**, and the outlet port P2 to an upper portion of the bowl interior for collecting separated fractions. A core **72** occupies a coaxial volume of the interior of bowl **12** and provides a separation volume between the coaxial wall of core **72** and the outer bowl wall **70**.

As bowl **12** is rotated, centrifugal forces separate the anticoagulated whole blood admitted into the bottom of the bowl into red blood cells (RBC), white blood cells (WBC), platelets and plasma. The blood is separated into different fractions in accordance with the component densities. The higher density components, i.e. RBCs **60**, are forced to the outer wall **70** of bowl **12** while the lighter density plasma **66** lies nearer the core **72**. A "buffy coat" **61** is formed between the plasma **66** and the RBCs **60**. The "buffy coat" **61** is made up of an inner layer of platelets **64**, a transitional layer **68** of platelets and WBCs and an outer layer of WBCs **62**. The plasma **66**, being the component closest the exit port from the separation volume, is the first fluid component displaced from bowl **12** via port PT2 as additional anticoagulated whole blood enters bowl **12** through port PT1.

Returning to FIG. **1A**, the exiting plasma passes through line sensor **14**, tubing **36**, 3-way T-connector **26** and valve V2 (in the open position) before entering air/plasma container **18**. Plasma entering air/plasma bag **18** is drawn from container **18** by recirculate/surge pump P2 and is recirculated at about 20–30 ml/min into bowl **12** through port PT1. The recirculated plasma dilutes the anticoagulated whole blood entering bowl **12** and allows the blood components to separate more readily. The equation for optimum recirculation rate is as follows:

$$Qr = Qc - \left[\left[1 + \left[\left[\frac{Hd}{100} \right] \cdot (ACD - 1) \right] \right] \cdot Qd \right]$$

where,

Qr=recirculation flow rate (ml/min.)

Qc=critical flow rate (ml/min.)

Hd=donor hematocrit (%)

ACD =ACD/anticoagulated whole blood ratio

Qd=Draw flow rate (ml/min.)

A critical flow rate of between 60 and 80 ml/min. has been shown to be effective at keeping platelet separated from WBC's. When a bowl optical sensor **21** senses the "buffy coat" is at a particular radius called the "surge" radius (≈3.81 cm), the DRAW cycle is completed. Valve V1 is closed, pump P1 is stopped so blood is no longer drawn from the donor and the DWELL stage is commenced.

During DWELL, pump P2 recirculates plasma **66** through bowl **12** at a moderate rate (about 100 ml/min as depicted in FIG. **2**) for about 20–25 sec. (331–354). At this flow rate, the "buffy coat" **61** widens but the platelets do not leave bowl **12**. The lowered concentration of particles in the "buffy coat" allows the heavier white cells to sediment to the outer side of the "buffy coat". The recirculated plasma maintains a constant flow rate of dilutant through the "buffy coat" (in the direction of the arrows) and results in a better separation between the lighter platelet layer **64** and the heavier white blood cell layer **62**. As a result, the transitional layer **68** is reduced. The DWELL period also allows the flow patterns

in bowl 12 to stabilize and allows more time for microbubbles to leave bowl 12 and be purged.

After DWELL, the SURGE stage is commenced. In SURGE, the speed of pump P2 (starting at 100 ml/min) is increased in 10 ml/min increments to recirculate plasma until reaching a platelet surge velocity of about 200 ml/min. The platelet surge velocity is the velocity at which platelets can leave bowl 12 but not red blood cells or white blood cells. The plasma exiting the bowl becomes cloudy with platelets and this cloudiness is detected by line sensor 14 (See FIG. 2, curve b) and the output of the detector decreases at point A. Line sensor 14 consists of an LED which emits light through blood components leaving the bowl 12 and a photo detector which receives the light after it passes through the components. The amount of light received by the photo detector is correlated to the density of the fluid passing through the line.

When platelets first start leaving the bowl 12, the line sensor output starts to decrease. At point A in curve b, FIG. 2, valve V3 is opened and valve V2 closed and the platelets are collected in container 20. Once the majority of the platelets are removed, from bowl 12, the fluid exiting the bowl becomes less cloudy. This lessening of cloudiness is detected by line sensor 14 and the line sensor output bottoms out at the inflection point B. At this point the total depth of the curve is taken, and the machine waits until the sensor signal rises for a given percentage, point C. At this point of time, the valve V3 is closed and the collection ended, or collection of white cells initiated.

Optionally, at this point C, collection of WBC may be started as indicated in FIG. 1A, utilizing an additional valve V4 and a third collection container, WBC bag 22 (shown in dotted lines in FIG. 1A). After the line sensor output has reached its minimum, inflection point B, the fluid starts to clear out. Once the sensor output has risen a given percentage, relative to the total depth of the curve, point C is reached and valve V3 is closed, valve V4 is opened and the recirculation pump further increases its speed to the lymphocyte surge rate. This initiates the collection of WBC. The line sensor will soon reach a maximum; the deflection point D. Once the deflection point has been reached, the cloudiness of the fluid will start to increase again as larger particles start to leave the bowl. The machine now waits for the sensor signal to drop to a given percentage of the original line sensor reference value; point E. At this point red cells start leaving the bowl and valve V4 is closed and collection is ended.

After the platelets and/or WBC have been collected, apparatus 10 begins the RETURN stage. During return, the rotation of bowl 12 is stopped and the remaining blood components in bowl 12 are returned to the donor (by reversal of rotation of pump P1) via phlebotomy needle 24 with valve V1 open. V2 is also opened to allow air to enter the centrifuge bowl during return. Plasma from container 18 dilutes the remaining blood components in bowl 12. Pump P2 mixes the plasma with the returning components in bowl 12 with valve V2 open diluting the returned components to speed up the return time. When the remaining blood components in the bowl have been returned to the donor, the RETURN stage is terminated and the phlebotomy needle 24 may be removed from the donor.

Depending upon the amount of platelets needed, this process of DRAW, DWELL, SURGE and RETURN can be performed multiple times.

During DRAW, the anticoagulated whole blood entering bowl 12 can be diluted with a solution such as saline from a container 90 (shown in dotted lines) instead of plasma using V6, V5, and pump P2.

An alternative two pump embodiment 50 of the present invention is shown schematically in FIG. 6. Apparatus 50 uses two pumps, draw/return pump P1 and an anticoagulant pump P3.

In operation, apparatus 50 is primed in the same manner as previously discussed. Apparatus 50 also performs the DRAW, DWELL, SURGE and RETURN stages in a similar manner to that of apparatus 10. FIG. 7 graphically shows the pump speeds for pump P1 for the DRAW, DWELL and SURGE stages. During the DRAW stage, whole blood is drawn from a donor and mixed with anticoagulant using pumps P1 and P3. Valve V1 is open, allowing anticoagulated whole blood to pass through tubing 28 and blood filter F1 before being pumped into bowl 12 through inlet port PT1. Bowl 12 is rotated, separating the anticoagulated whole blood into different fractions. The least dense component, i.e. plasma 66, is the first displaced from bowl 12 via port PT2 as additional anticoagulated whole blood enters bowl 12 through port PT1. The plasma passes through tubing 36, is sensed by line sensor 14 and completed through T-connector 26 and through valve V2 (in the open position) and enters container 18. Valve V5 is closed, permitting the plasma to collect in container 18. After the bowl optics 21 sense the "buffy coat" is at the proper position, valve V1 closes, terminating the DRAW stage.

Apparatus 50 then begins the DWELL stage. During DWELL, pump P1 pumps collected plasma from container 18 (with valve V5) open into bowl 12 through tubing 34 and port PT1 at an elevated rate of 120 ml/min for a period of about three seconds before dropping to a moderate 75 ml/min for about 27 more seconds (FIG. 7). The plasma 66 flows through the "buffy coat" and dilutes it. The three second period of elevated flow rate thus widens the thickness of "buffy coat" thereby providing a better separation between platelets and WBCs. The remaining period at the moderate flow rate stabilizes the flow patterns in bowl 12. After DWELL, pump P1 increases the flow rate of the recirculating plasma at the rate of 8 (ml/min)/sec until reaching the maximum surge velocity of 200 ml/min (FIG. 7). At the maximum surge velocity, platelets (FIG. 3) begin to exit bowl 12. The plasma exiting the bowl 12 becomes cloudy with platelets and this cloudiness is detected by line sensor 14. Line sensor 14 causes valve V3 to open and the platelets are collected in container 20. After the platelets have been removed from bowl 12, line sensor 14 detects the absence of platelets and closes valve V3.

Optionally the WBC collection stage can be commenced using values V4 and WBC by 22 (shown in dotted lines) after which the RETURN stage is commenced. The rotation of bowl 12 is slowed and the remaining blood components in bowl 12 are returned to the donor by pump P1 via phlebotomy needle 24.

FIG. 4 depicts a prior art product sold by Haemonetics Corporation under the name Mobile Collection System (MCS). This system 10' physically is similar to the present system and has the surge capability of the prior out patient referenced supra. In this system the branching connector 26' is located upstream of the optical sensor 14'. Outlet port PT2' is in fluid communication with tubing 36' and Y-connector 26'. One branch of tubing 36' passes through optical sensor 14'. M2' is coupled directly to pressure monitor M2' via tubing 38'. This prior art location of Y-connector 26' causes foam, which is floating on the surface of blood components leaving bowl 12' through port PT2' to substantially mix with the separated components. The mixing of the foam with the components results in false readings from the optical line sensor 14' because the mixed foam scatters light emitted by

the LED of line sensor **14'** so that the photo detector does not receive the correct amount of light associated with the specific blood component exiting bowl **12'**. False reading can cause less than optimal component collection i.e., less platelets are collected than is desired.

FIG. **5** depicts the location of a T-connector **26** downstream of line sensor **14** in the apparatus **10** of the present invention. As may be seen, T-connector **26** is disposed between the line sensor **14** and container **18** and monitor M2 ensuring that an uninterrupted length of tubing **36** is present between port PT2 and the line sensor **14**. The uninterrupted tubing **36** reduces the possibility that foam floating on fluid exiting bowl **12** will be substantially mixed with the exiting fluid causing line sensor **14** to make false readings.

Referring back to FIG. **1B** and the disposable set depicted therein it should be noted that the length of tubing **36** between PT2 and T-connector **26** must be sufficient to permit T-connector **26** to extend downstream beyond the location of the line sensor **14** (FIG. **5**).

Furthermore, use of a so-called "chimney bag" **18** is recommended for the air/plasma application. Chimney bag **18** has a top port PT3 for introduction of air or plasma and a bottom port PT4 coupled via tubing to Y-junction **91** and either to input port PT1 for surge purposes or to phlebotomy needle **24** through filter F1 for fast return purposes. Sterile air from bowl **12** is stored temporarily in the air/plasma bag **18**, rather than the conventional use of an air/platelet bag for air storage. By entering the air into the plasma/air bag rather than the platelet bag, the lines **36**, **37**, **39** and **35** from the bowl **12** to the bags are cleaned out into the plasma bag. This means that any contamination (i.e. WBC's) in the lines will not be drained into the platelet component product. This results in a lower white cell count of the platelet product.

In the DWELL and SURGE stages the chimney bag **18** operates as an air trap; this reduces foaming in the bowl **12** and thus more stable line sensor outputs.

FIGS. **8A** and **8B** are a processing flow chart indicating the major steps required to process blood and collect platelets in accordance with the apparatus of the invention. In the flow chart the following terms have the meanings given in Table I below:

TABLE I

Term	Definition
B.O.	Bowl Optics
Ref.	reference
L.S.	line sensor
Recirc. speed	speed of recirculation pump
CLEAR B.O. REF	Bowl optics voltage off empty bowl
AIR/PLASMA INTERFACE	Bowl Optics detects fluid
COLLECTING PLASMA	Plasma collected through plasma valve
B.O. REF. TAKEN	Bowl Optics voltage off plasma in bowl
L.S. REF. 1	Line sensor voltage off plasma taken during Draw cycle
DWELL	Draw pump stops. Plasma recirculated at 100 ml/min through bowl
L.S. REF. 2	Line sensor voltage of f plasma taken during DWELL cycle
Start Collection	Close plasma valve. Open platelet valve. Start collecting platelets
Peak value	Lowest voltage value measured by line sensor

While the bowl is being filled a display on a control panel (**100**, FIG. **5**) displays "FILLING BOWL" and after 40 ml of anticoagulated whole blood has been pumped by pump P1 into bowl **12** a reading is taken using an optical detector (called the Bowl Optics) located adjacent transparent centrifuge bowl **12**. If this reading is less than 50% of an optically clear reference reading with the bowl empty; then the display indicates that fluid has been detected by displaying an AIR/PLASMA Interface signal. If not, a new reading is taken (STEP1).

After another 55 ml has been pumped into the bowl the display indicates that plasma is now being collected and a plasma B.O. reading is taken of the plasma as it forms in the bowl (STEP2). If this reading is less than 80% of a plasma reference reading then a line sensor reading is taken of the plasma during a draw cycle. If not, then step **2** is repeated.

After the line sensor reading is taken (STEP3) another BO reading is taken until the bowl optics reading indicates that the value is less than 65% of the BO plasma reference reading, in which case, the DWELL stage is commenced (STEP4).

After 25 sec. of DWELL a second line sensor reference reading is taken (STEP5). At 30 sec. of DWELL, the line sensor reference **2** value is compared with the line sensor reference **1** value. If L.S. REF **2** is greater than 92% of the L.S. REF **1**, then the L.S. REF. **2** value is used as a reference in the next step. If not, then the L.S. REF. **1** value is used (STEP **6**).

Next, the SURGE stage is entered by increasing the recirculation speed of Pump P2 in increments of 10 (ml/min)/sec and the line sensor reading is compared with the L.S. REF reading selected in STEP6. If the reading is less than 95% of the reference value and the pump speed is greater than 150 ml/min platelet collection is commenced and timer T(1) is started (STEP **7**).

When the recirculation speed is equal to 200 ml/min the speed is kept constant at 200 ml/min. If T(1) is less than or equal to 2 seconds and the slope of the Line Sensor curve (curve b of FIG. **2**) is greater than or equal to zero, the peak value of the LS curve is stored and timer T(2) is started. If T(1) is greater than 2 seconds and the LS slope is not greater than or equal to zero, platelet collection is terminated (STEP **8**).

Timer T(2) starts and runs until T(2) is equal to 1.5 second. If over 6 sampling intervals the L.S. output increases by less than +5 digital values over each interval then platelet collection is terminated. If not, the collection is ended when 50% of the difference between the line sensor reference voltage and the line sensor minimum voltage is reached (STEP **9**).

A simplified revision of the line sensor curve b is shown in FIG. **9** to summarize the platelet collection process described above. In FIG. **9** the output of line sensor **14** is plotted versus time for a typical platelet collection process in accordance with the invention. At point A a Line Sensor Reference voltage is taken from the average value calculated at 25–30 sec. into DWELL. Surge is commenced at point B. Platelet collection is commenced when the Surge Speed is greater than 150 ml/min., and the line sensor voltage is less than 95% of the Line Sensor Reference voltage. The slope reversal at point C is detected and the slope is monitored until it levels off or decreases in which case platelet collection is ended. If the slope is increasing then collection is continued until the Line Sensor voltage reaches 50% of the reference value.

While this invention has been particularly shown and described with references to the preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention as defined by the appended claims.

We claim:

1. A method of increasing intermediate density blood component yield from donated whole blood in a centrifugation fractionation volume, the intermediate density component consisting primarily of at least one of a platelet constituent and a white blood cell constituent, the method comprising the steps of:

(i) diluting whole blood, by mixing fluid with the whole blood at a first flow rate as the blood is introduced into the volume;

(ii) separating lower density component in the volume from higher density components in the volume including said intermediate density component, and displacing said lower density component to a first container;

(iii) recirculating the lower density component to the volume at a second, substantially constant flow rate to further dilute the components remaining in the volume and widen the region occupied by said intermediate density component without causing said intermediate density component to exit the fractionation volume;

(iv) recirculating the lower density component through the volume at a third, accelerating flow rate; and

(v) displacing said intermediate density component from the volume while the lower density component is recirculating through the volume at the third flow rate.

2. The method of claim 1 wherein the components remaining in the bowl after (v) are reinfused.

3. The method of claim 1 wherein the second flow rate is greater than the first flow rate.

4. The method of claim 1 wherein the third flow rate is greater than the second flow rate.

5. The method of claim 1 further comprising collecting the intermediate density component in a second container.

6. The method of claim 5 further comprising anticoagulating the whole blood with anticoagulant stored in a third container.

7. The method of claim 6 wherein said intermediate density component consists primarily of platelets and wherein the method further comprises displacing white blood cells from the volume and collecting the white blood cells in a fourth container.

8. The method of claim 1 in which said intermediate density component consists primarily of platelets.

9. The method of claim 1 wherein said intermediate density component consists primarily of white blood cells.

10. The method of claim 1 wherein said intermediate density component consists primarily of platelets and white blood cells.

11. A method of increasing intermediate density component yield from donated whole blood in a centrifuge having an enclosed fractionation volume, the intermediate density component consisting primarily of at least one of a platelet constituent and a white blood cell constituent, the method comprising:

(i) pumping whole blood into the volume along a first flow route;

(ii) separating lower density component in the volume from higher density components in the volume including said intermediate density component, and displacing the lower density component to a first container;

(iii) closing the first flow route and opening a second flow route, and returning the lower density component to the volume at a first, substantially constant flow rate to widen the region occupied by said intermediate density component without causing said intermediate density component to exit the fractionation volume;

(iv) recirculating the lower density component through the volume at a second, accelerating flow rate; and

(v) displacing said intermediate density component from the volume while the lower density component is recirculating though the volume at the second flow rate.

12. The method of claim 11 wherein the components remaining in the bowl after (v) are reinfused.

13. The method of claim 11 wherein the second flow rate is greater than the first flow rate over an entire range of acceleration of the second flow rate.

14. The method of claim 11 further comprising collecting the intermediate density component in a second container.

15. The method of claim 14 further comprising anticoagulating the whole blood with anticoagulant stored in a third container.

16. The method of claim 15 wherein the intermediate density component comprises primarily platelets and the method further comprises displacing white blood cells from the volume and collecting the white blood cells in a fourth container.

17. The method of claim 11 in which said intermediate density component consists primarily of platelets.

18. The method of claim 11 wherein the lower density component initially returns to the volume at a flow rate which exceeds the first flow rate before slowing to the first flow rate.

19. The method of claim 11 wherein said intermediate density component consists primarily of white blood cells.

20. The method of claim 11 wherein said intermediate density component consists primarily of platelets and white blood cells.

21. A method of increasing component yield from donated whole blood in a centrifuge having an enclosed fractionation volume, the method comprising:

(i) pumping into the volume anticoagulated whole blood having components of varying density including an intermediate density component which consists primarily of at least one of a platelet constituent and a white blood cell constituent;

(ii) separating lower density component in the volume from higher density components including said intermediate density component in the volume and displacing the lower density component to a first container;

(iii) returning the lower density component to the volume at a first, substantially constant flow rate to dilute components remaining in the volume and widen the region occupied by said intermediate density component without causing said intermediate density component to exit the fractionation volume;

(iv) recirculating the lower density component through the volume at a second, accelerating flow rate; and

(v) displacing said intermediate density component from the volume while the lower density component is recirculating through the volume at the second flow rate.

22. The method of claim 21 wherein the components remaining in the bowl after (v) are reinfused.

23. The method of claim 21 further comprising collecting said intermediate density component in a second container.

24. The method of claim 23 further comprising anticoagulating the whole blood with anticoagulant stored in a third container.

25. The method of claim 24 wherein said intermediate density component consists primarily of platelets and the method further comprises displacing white blood cells from the volume and collecting the white blood cells in a fourth container.

26. The method of claim 24 wherein said intermediate density component consists primarily of platelets.

27. The method of claim 24 wherein the lower density component initially returns to the volume at a flow rate which exceeds the first flow rate before slowing to the first flow rate.

28. The method of claim 24 wherein the whole blood is diluted with lower density component recirculating at a low flow rate before reaching the volume, the low rate being less than the first flow rate.

29. The method of claim 21 wherein said intermediate density component consists primarily of white blood cells.

30. The method of claim 21 wherein said intermediate density component consists primarily of platelets and white blood cells. hite blood cells.

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